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Fig. 1.

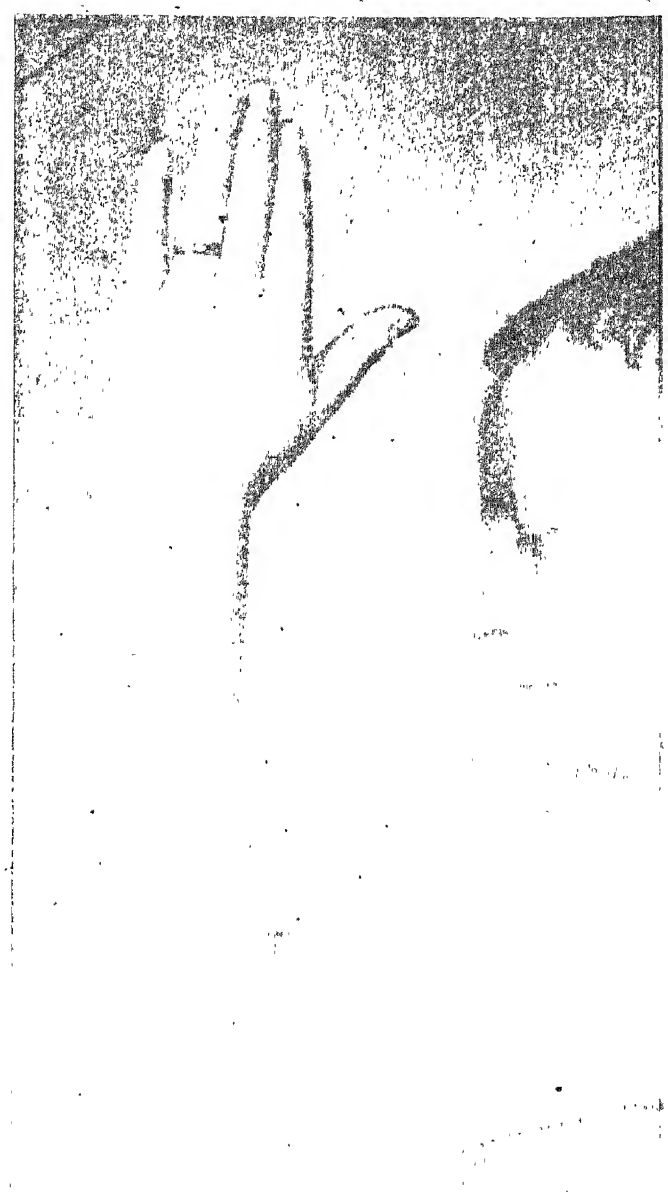
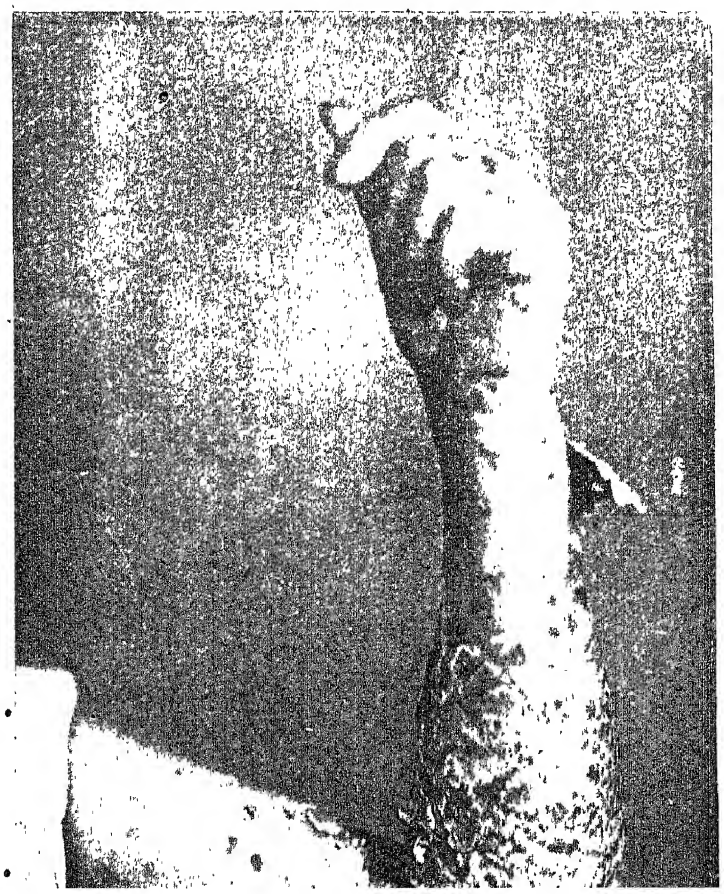
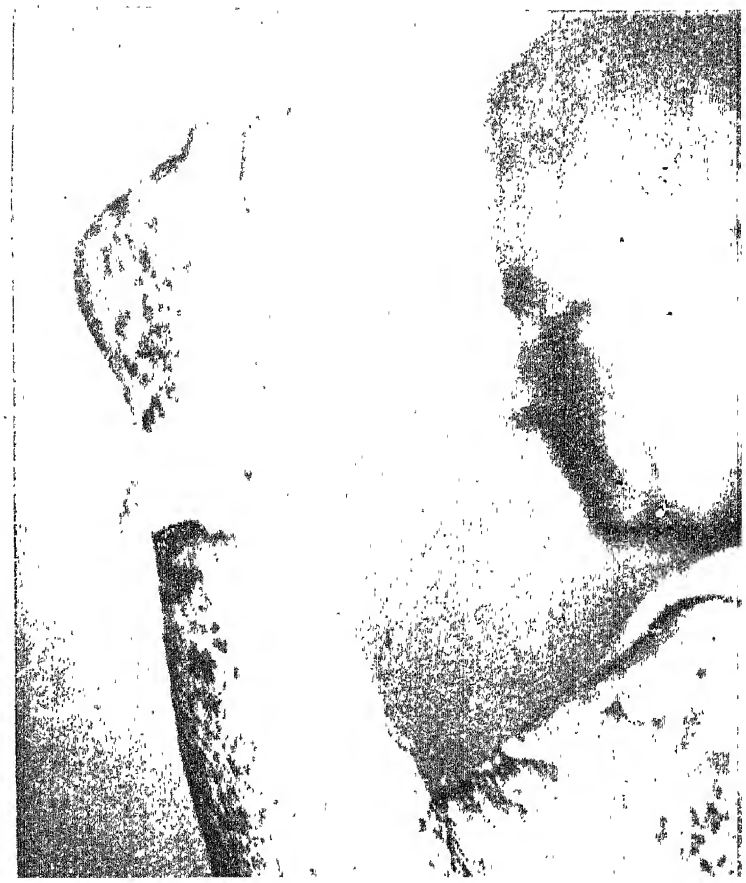


Fig. 4.





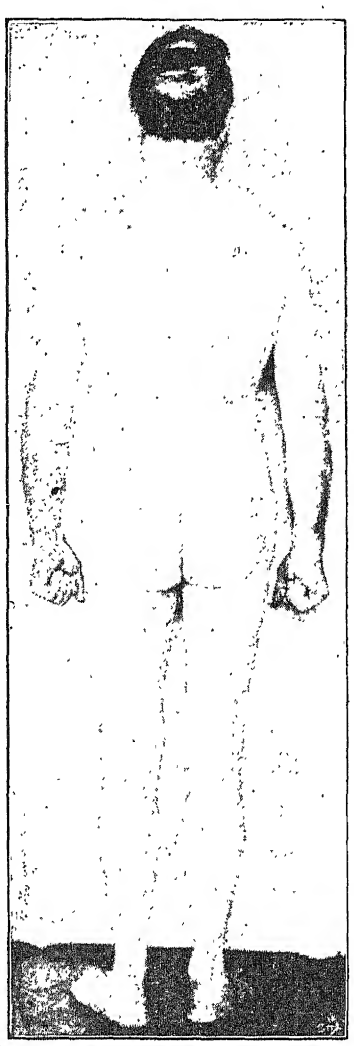


FIG. 1.

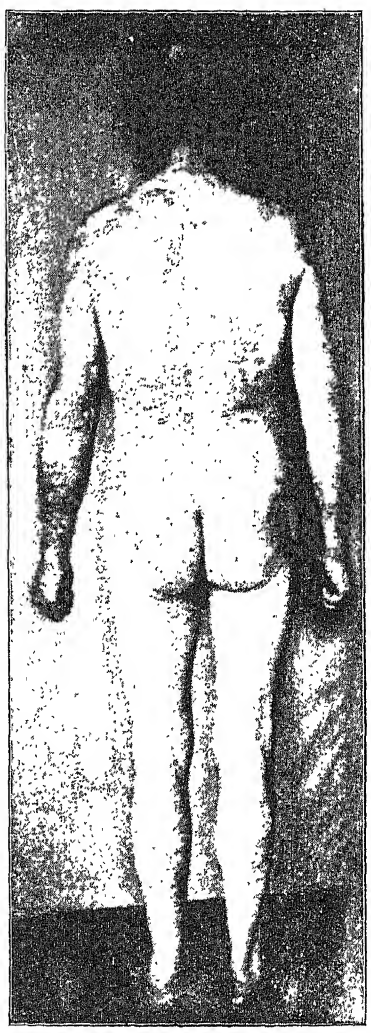


FIG. 2.

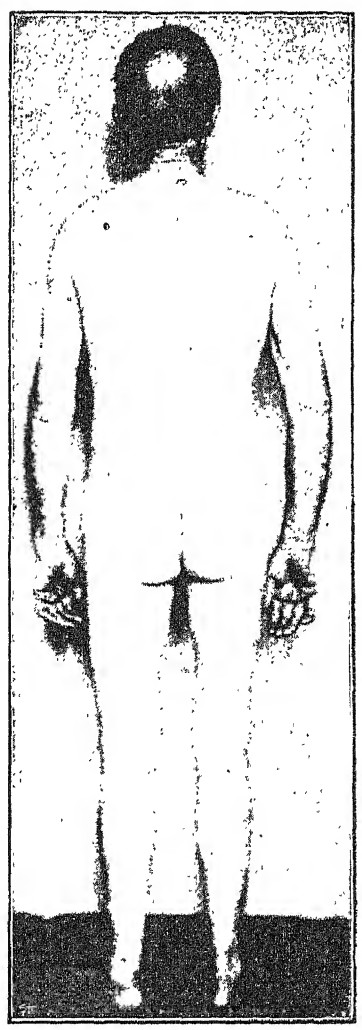
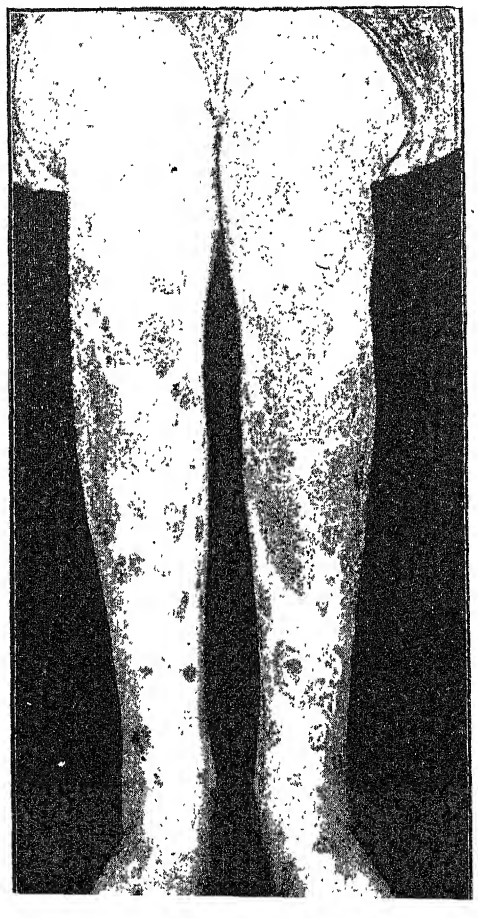


FIG. 3.

PSORIASIS (CASE OF J. C.) SHOWING THE CONDITION BEFORE, DURING, AND AFTER THYROID TREATMENT



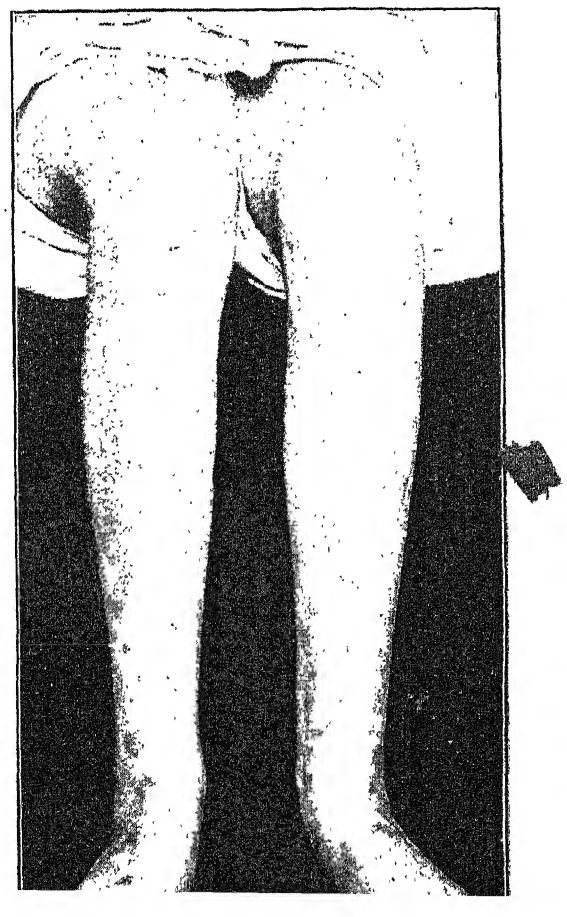


Fig 4

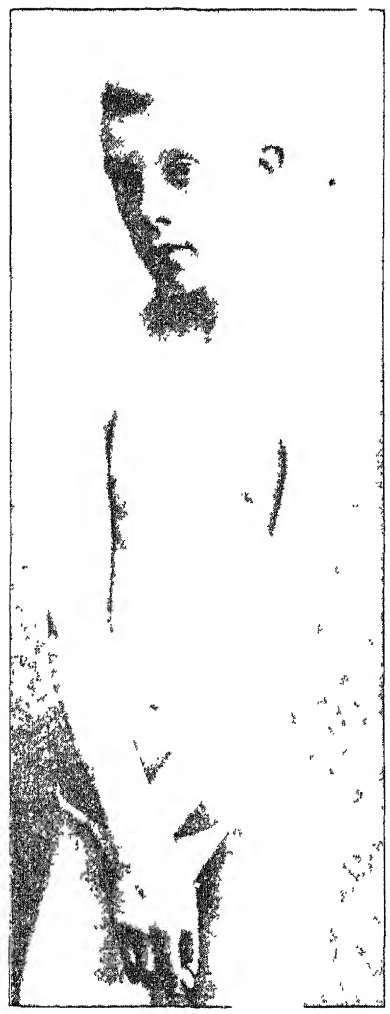


Fig 5

DR LENNOX'S CASE OF PSORIASIS (J W) SHOWING THE CONDITION BEFORE AND AFTER THYROID TREATMENT

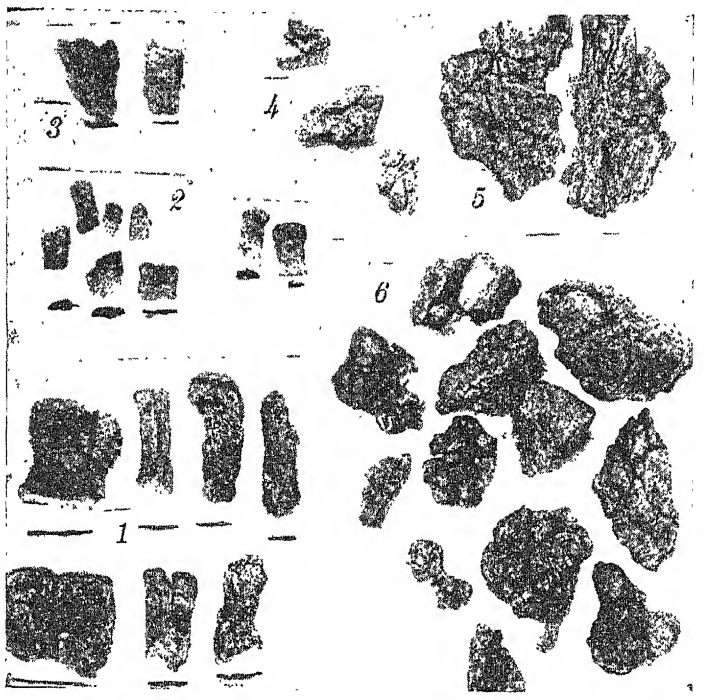


FIG. 4.—Scales detached from case of ichthyosis during thyroid treatment. Natural size.

1. Scales from the feet seen sideways (their attached ends are opposite the ink lines).
2. Scales from the inner side of arm seen sideways (their attached ends are opposite the ink lines).
3. Scales from the front of the abdomen seen sideways (their attached ends are opposite the ink lines).
4. Scales from the front of the knee (seen from the front).
5. Coherent mass of scales from outer surface of hip.
6. Individual scales from the dorsum of the foot and toes (seen from the front).

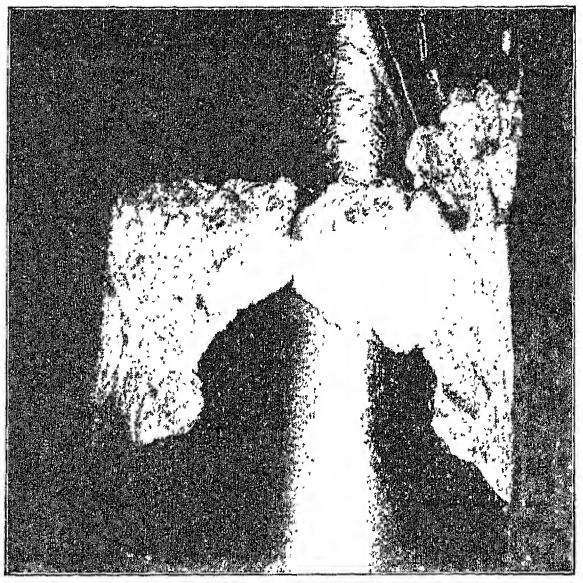
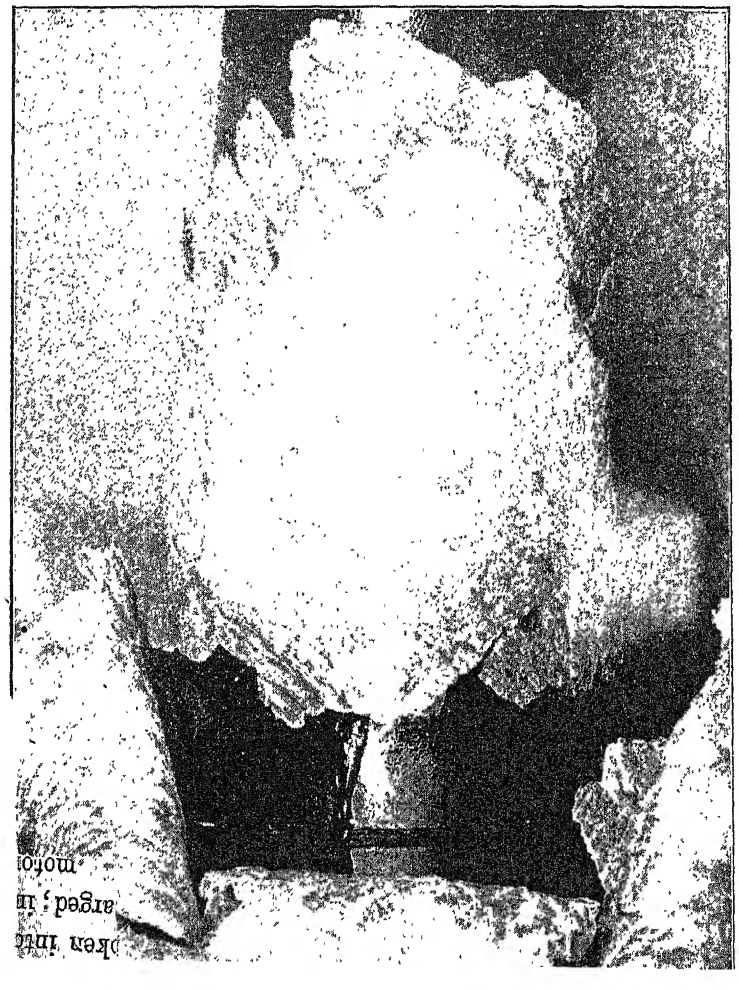


FIG. 2.—The back of the largest scale shown in fig. 1. It formed a complete circle of the wrist. In the photograph it is fixed round a roll of black paper.



DR. BYROM BRAMWELL

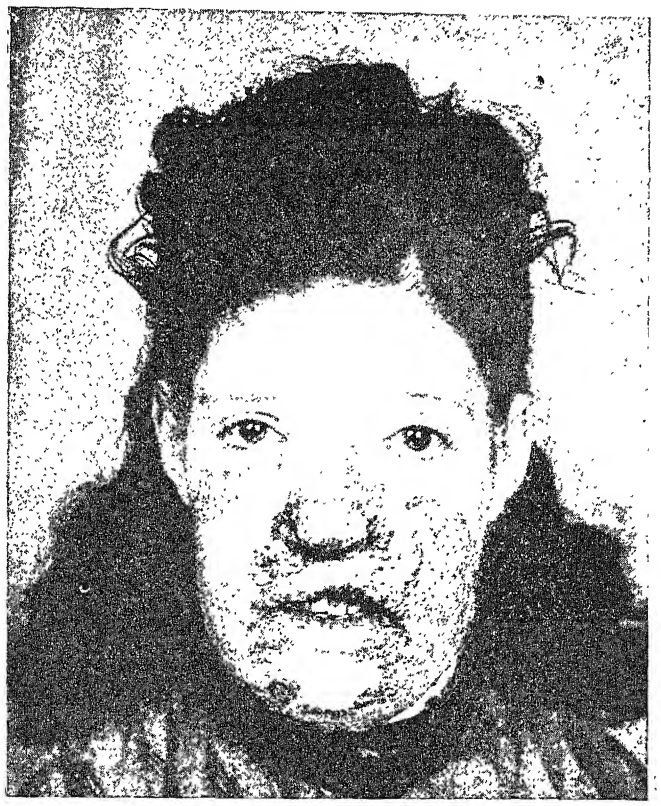


FIG. 1.

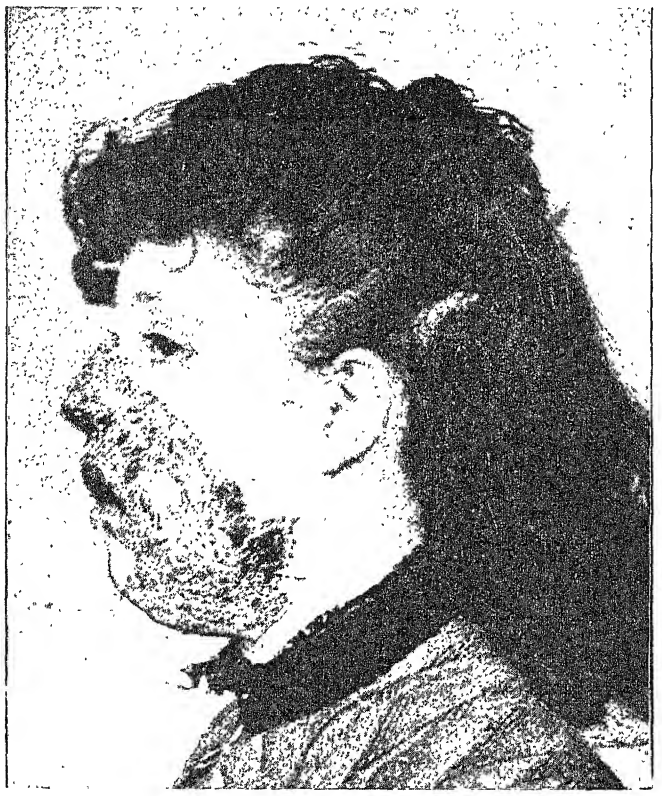


FIG. 2.

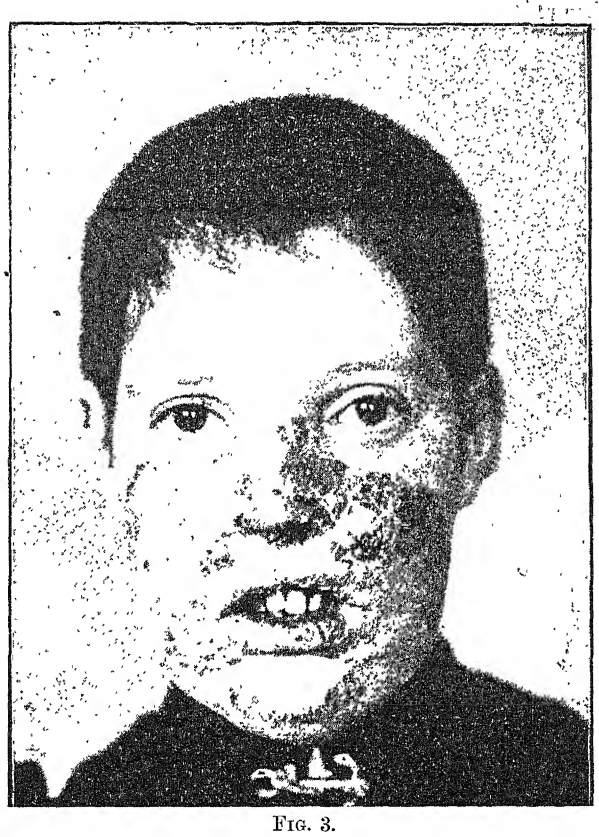


FIG. 3.

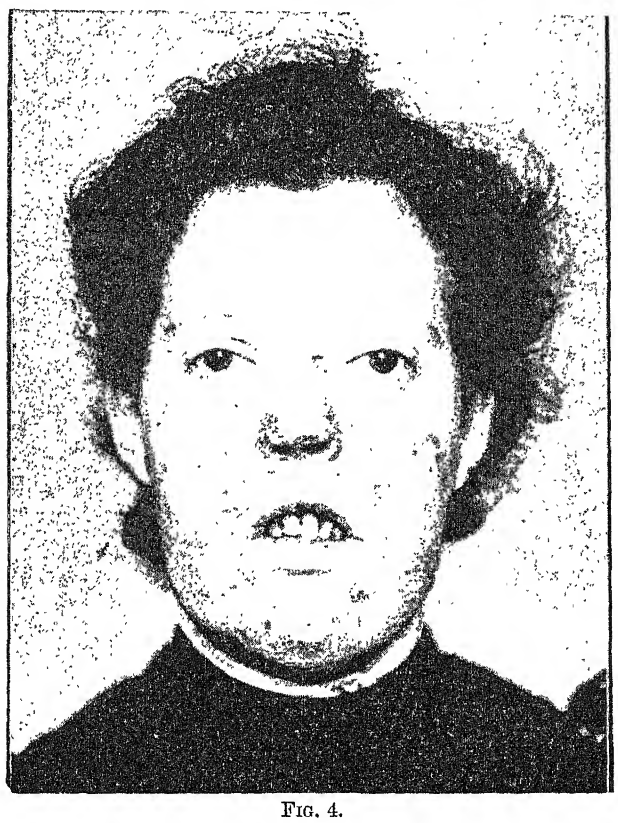


FIG. 4.

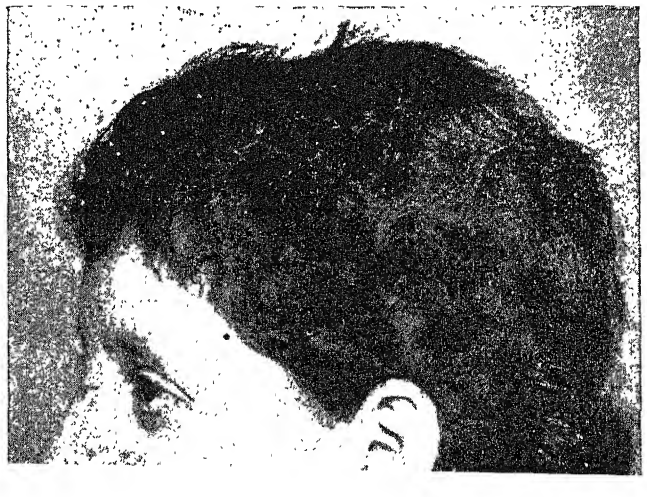


Fig. 1.

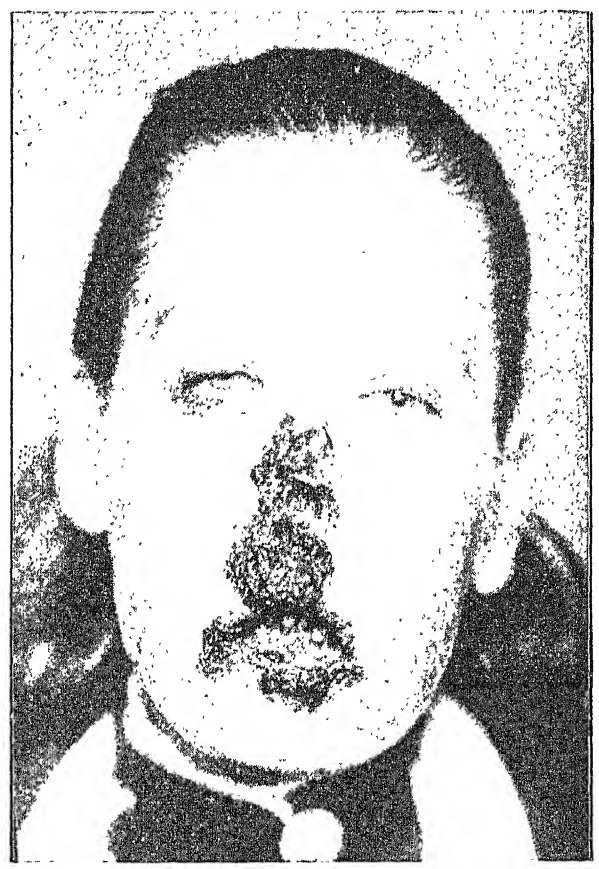
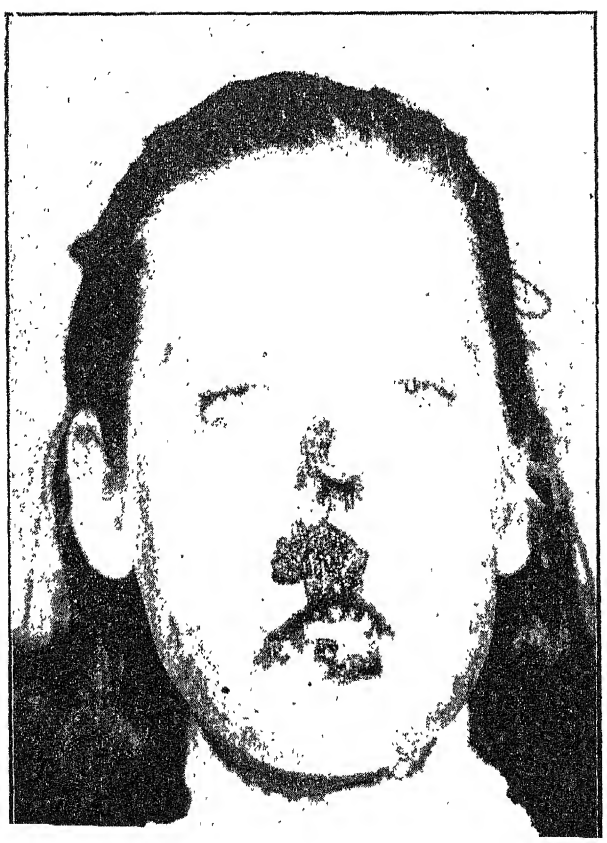


Fig. 2.



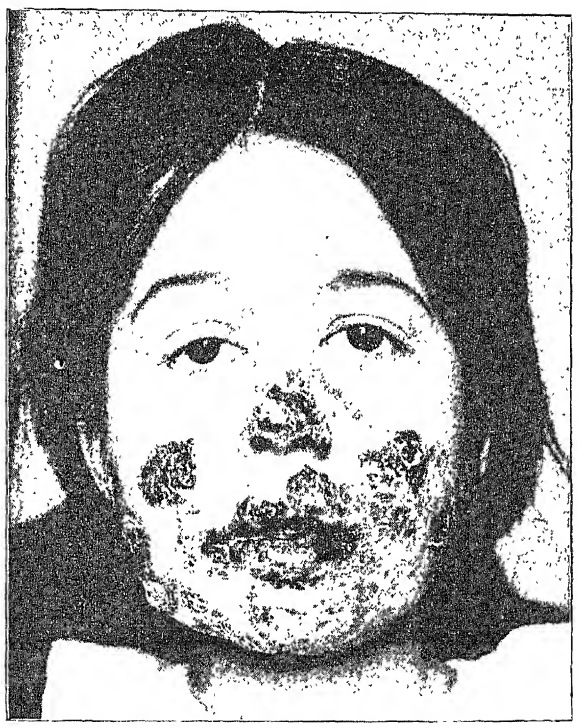


FIG. 3.

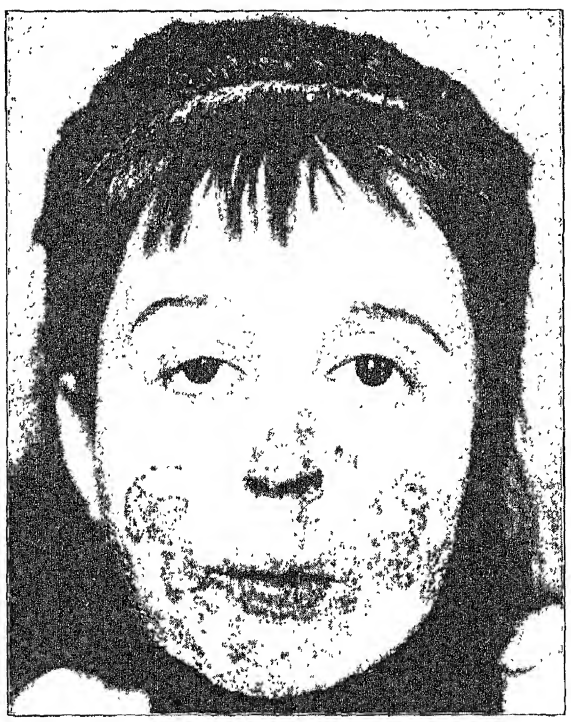


FIG. 4.

Figs. 3 and 4. LUPUS (CASE OF I. S.) TREATED BY THYROID EXTRACT, SHOWING THE APPEARANCE OF THE FACE ON MARCH 22nd AND JUNE 15th, 1894

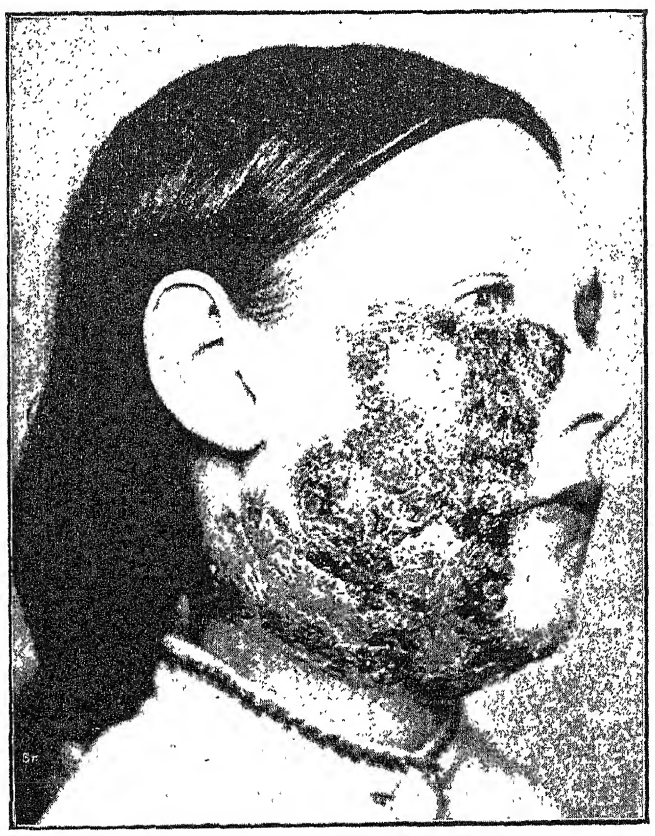


FIG. 1.

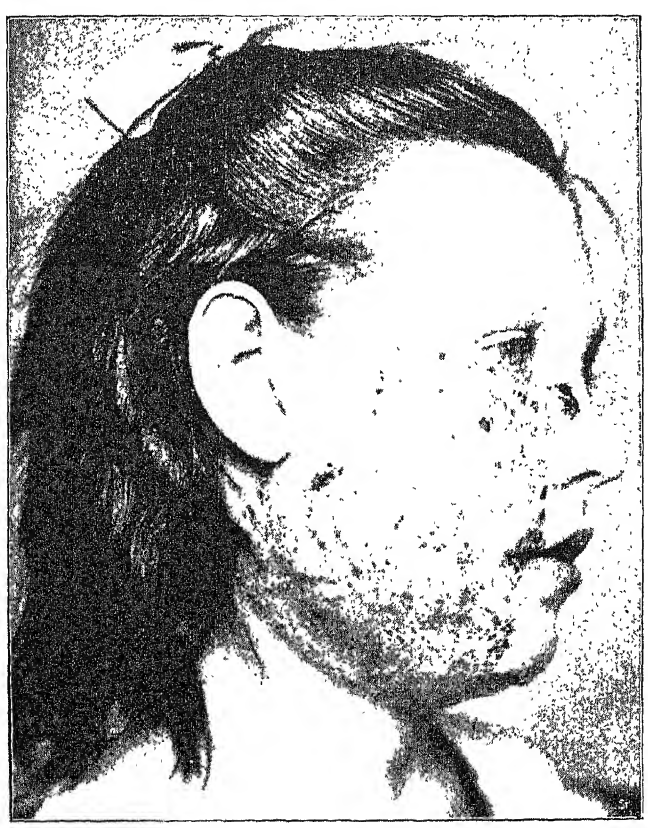
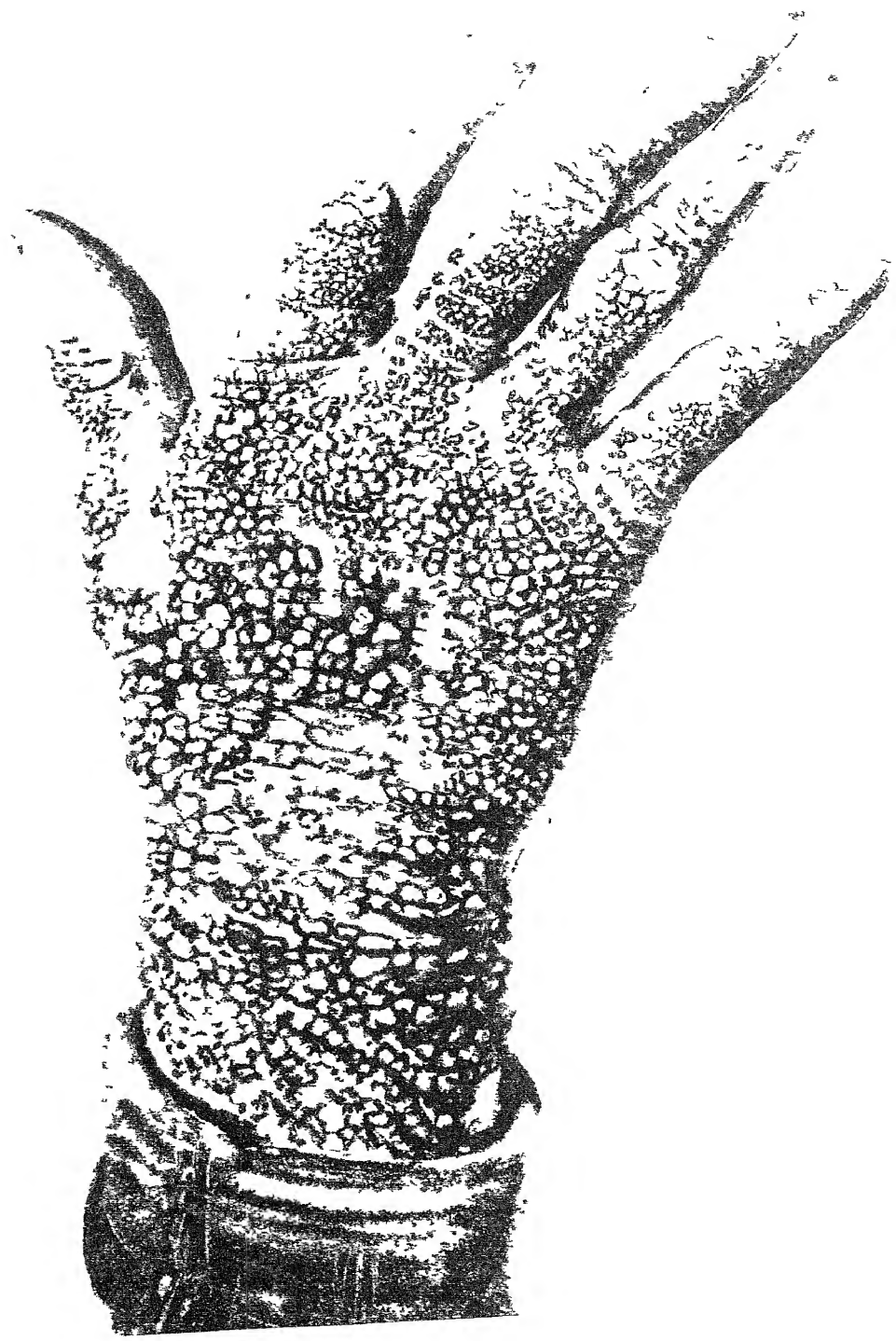


FIG. 2.



HAND Back and Front View from Case of ICHTHYOSIS

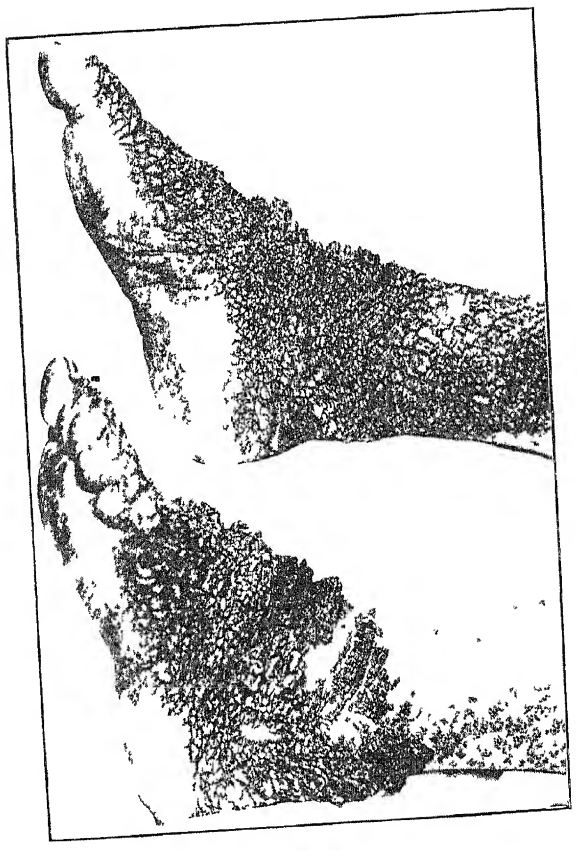
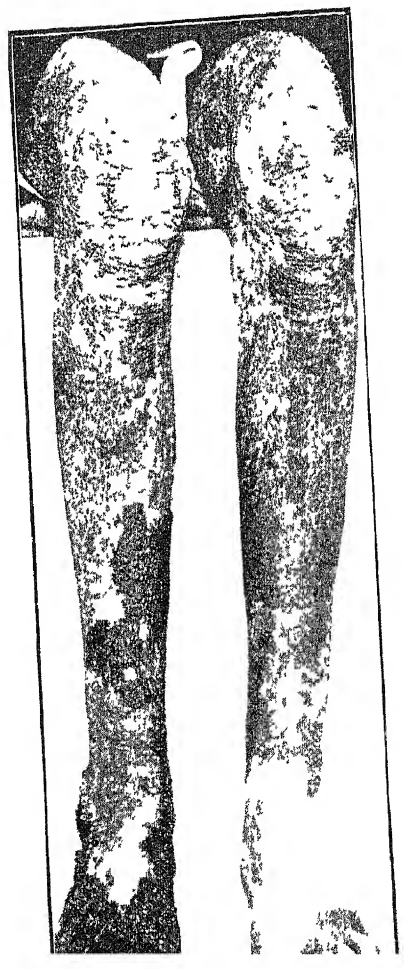
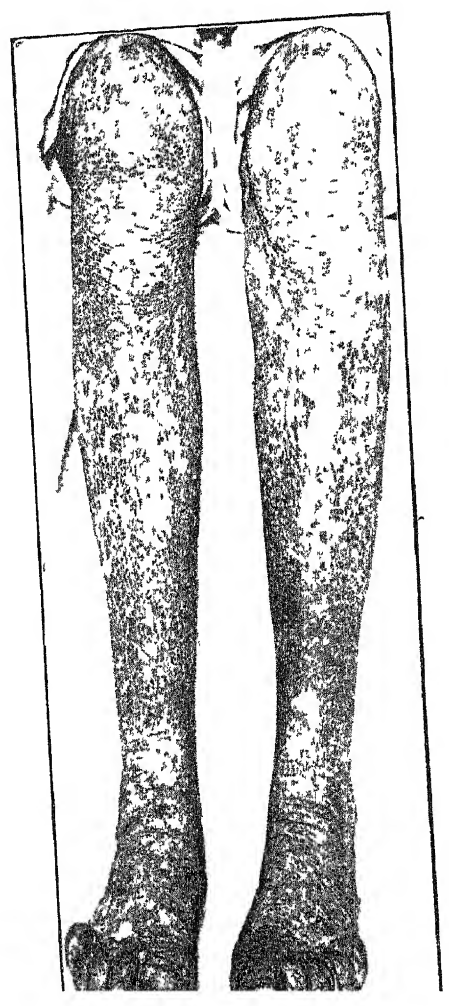


FIG 1

FIG 5





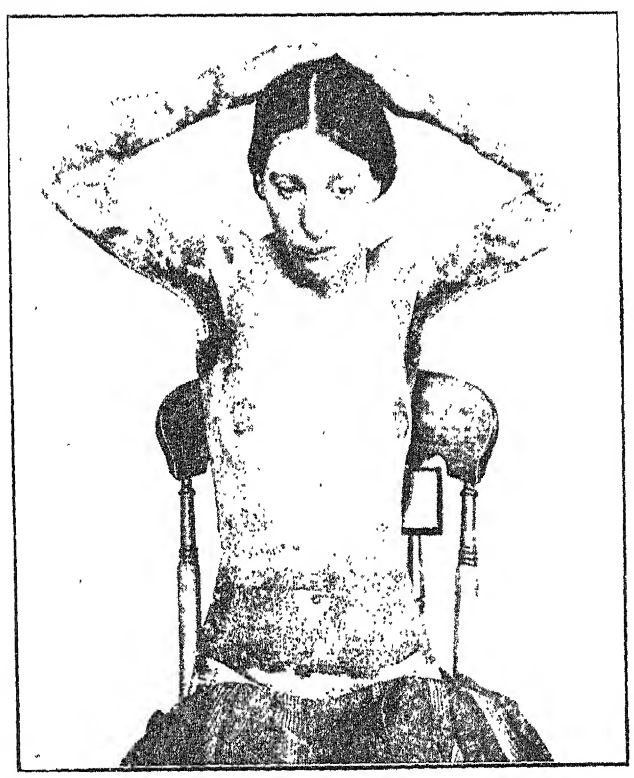


FIG. 1.

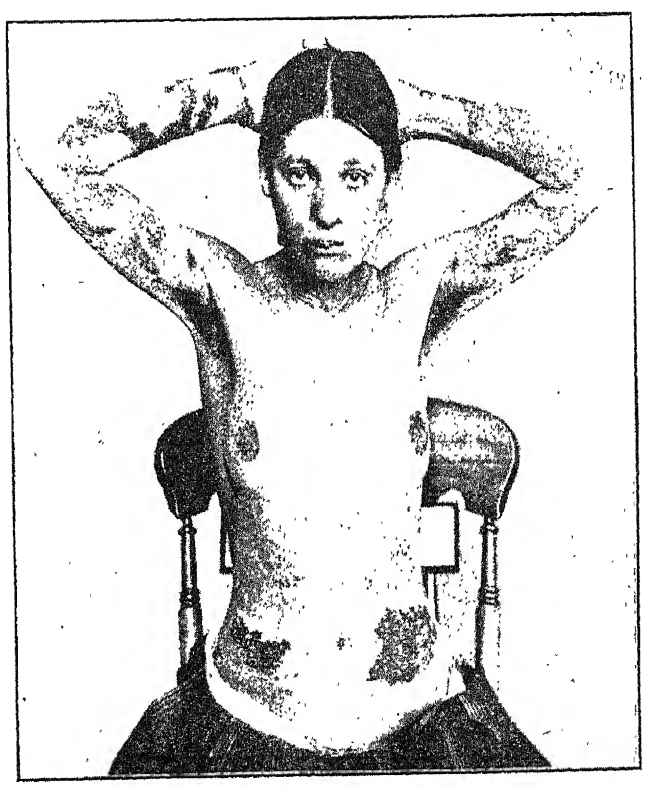


FIG. 2.

FIG. 3.

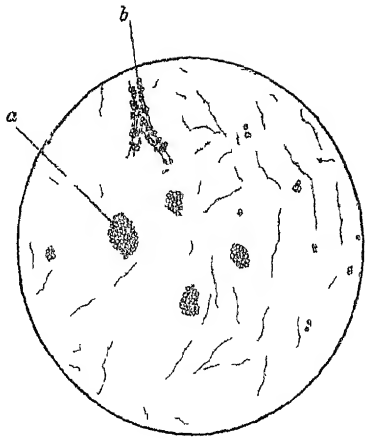


FIG 3.—Portion of the Anterior Horn of grey matter represented in fig 2, showing the minute structure of the lesion (osmic acid and farrant) more highly magnified

The dull particles *a* seen in fig 2 are fatty globules stained with osmic acid They are situated in spaces which have formerly contained nerve cells A small vessel *b* is seen at the upper part of the section—some fatty globules adhere to its outer coat

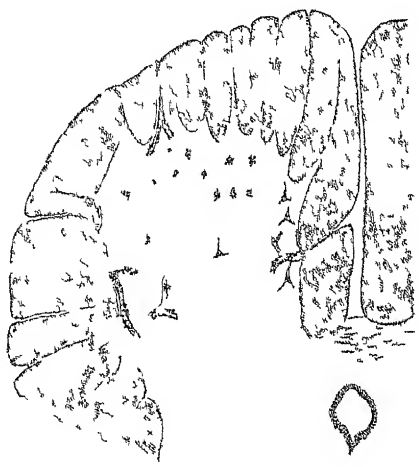
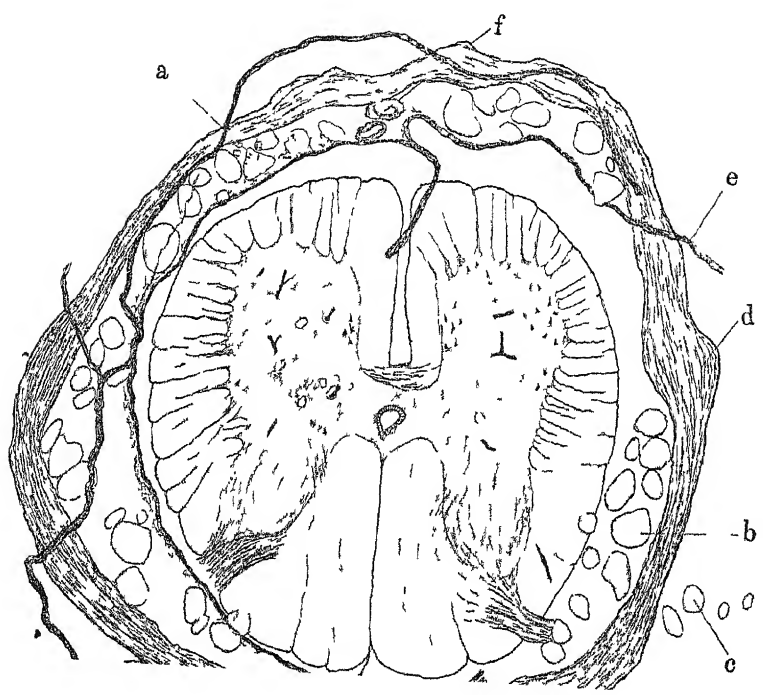


FIG 2.—Transverse section through the Anterior Horn of grey matter in a case of Infantile Paralysis (osmic acid and farrant), magnified about 15 diameters

Nearly all the nerve cells have disappeared Their place is taken by fatty particles which can be easily seen even with this low power



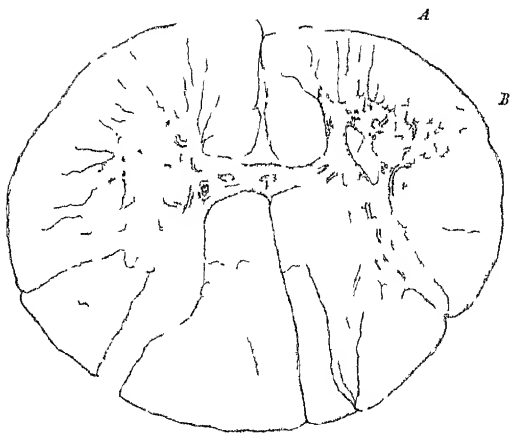


FIG 6.—Transverse section through the cervical region of the Spinal Cord in an old standing case of poliomyelitis anterior acuta, showing a cavity (*A*) in the right anterior horn of grey matter

There is some sclerosis (to which the letter *B* points) in the adjacent white columns which are atrophied The blood vessels in the grey matter of the left anterior horn of grey matter are dilated

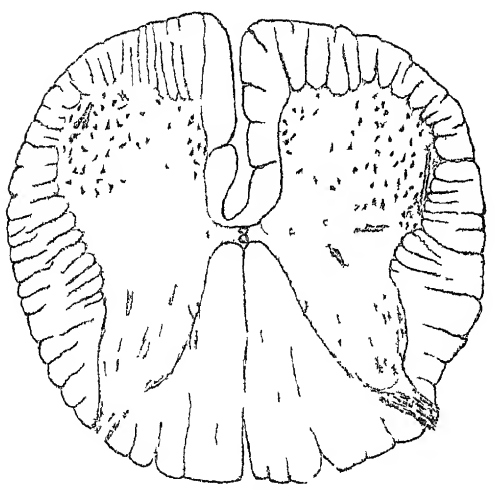


FIG 4.—Transverse section through the Lumbar Region of the Spinal Cord of a child, showing the normal appearance of the Anterior Cornua (carmine and dammar) magnified about 10 diameters

Numerous multipolar nerve cells are seen in the anterior horn The central canal is dilated This condition is rare and not of any practical importance

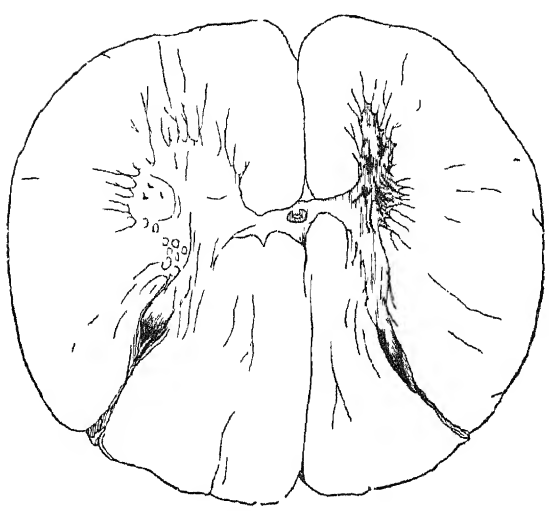
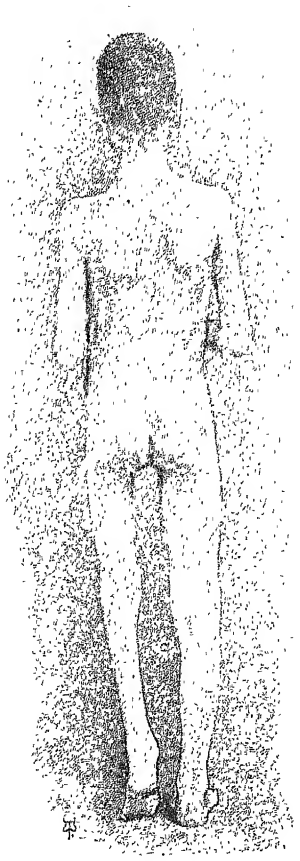
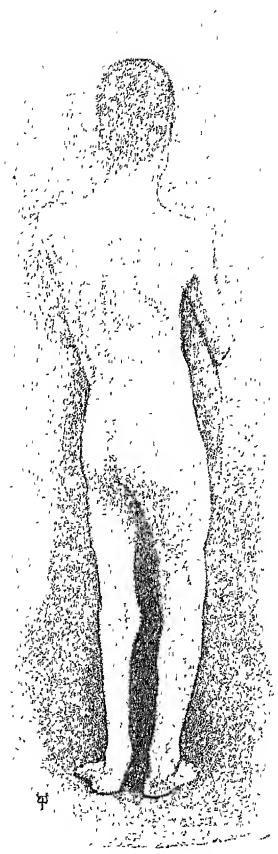
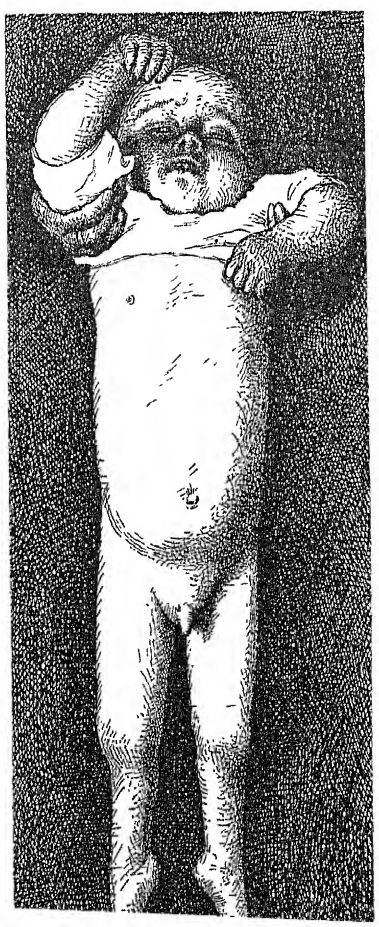


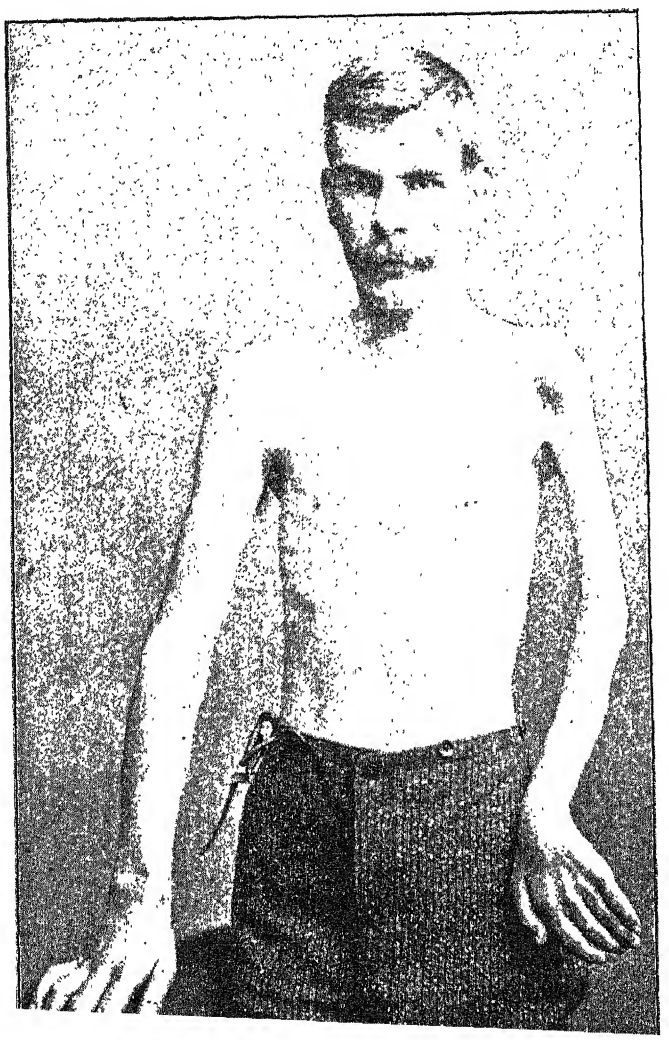
FIG 5.—Transverse section of the cervical region of the Spinal Cord in a case of old poliomyelitis anterior acuta (After Charcot)





FIGS. 3 and 4.—Poliomyelitis anterior acuta; paralysis and atrophy of the left leg; the muscles below the knee are more affected than those of the hip and thigh.





HEREDITARY OR CONGENITAL SYPHILIS

CASE OF GUMMA OF THE MEDULLA OBLONGATA

THE case which is represented in Plate LXXXII., fig. 1, is of great interest.

The patient, a boy six years of age, was sent to me on the 21st of March, 1893, by Dr. Cowan Guthrie of Leith, suffering from severe headache, right hemiplegia, paralysis of the tongue and difficulty in swallowing. The tongue was atrophied and wrinkled and was the seat of irregular fibrillary movements or twitchings.

Previous History.—On enquiry, I found that the patient had been quite well until December, 1891. He was at that time laid up for a month with a severe attack of influenza; he has never been well since. After the influenza, he became pale and thin and began to suffer from headache and vomiting. The vomiting usually occurred in the morning before breakfast, *i.e.* before he had taken any food. The headache and vomiting continued until the 12th of November, 1893, when he had a severe attack of measles, followed by bronchitis and inflammation of the lungs.

His mother stated that, during the week which preceded the development of the measles, he gradually lost the power of using his right hand; this was so noticeable that on more than one occasion his father said to her, 'I think that boy is going to be left-handed.'

During the attack of measles, the paralysis of the right arm increased and the right leg became affected; a squint developed; articulation became impaired, water ran out of his mouth and he had difficulty in swallowing.

After the eruption of measles disappeared, he was very ill for several weeks with bronchitis and pneumonia. During this time, the difficulty in swallowing increased; liquids used to choke him, unless swallowed with great care; they sometimes came out of his nose. His mother says that at this time his cough was very peculiar. Her own words were: 'His cough was the most peculiar I ever heard; it almost used to choke him because of the paralysis of the tongue.'

After the patient recovered from the bronchitis and pneumonia, his general health improved; he ate well and gained flesh, but his right arm and leg remained paralysed. His mother's description of the improvement was expressive but peculiar. Her words were:—'I knew the awfullest odds alive in him since he got better from the measles.'

About the beginning of February, 1893—that is to say, a [illegible] the apparently as the result of giddiness. Swallowing was difficult and articulation considerably impaired.

Present Condition.—When the patient came under my notice on March 21st, 1893, his general health appeared to be good; though rather pale, he was fat and well nourished. A point I wish particularly to emphasise is, that the facial appearance was in no way suggestive of inherited syphilis.

The movements of the right hand and arm were very much impaired; the right leg was dragged and circumducted and the fingers of the right hand were drawn into the palm. The right knee-jerk was exaggerated, while the plantar reflex was more marked on the left than on the right side. The muscles of the right (paralysed) arm and leg were firm and well nourished. Voluntary movements of the right arm were attended with a rhythmical tremor exactly like that of disseminated (cerebro-spinal) sclerosis.

At this, his first, visit, I thought that the muscles on the left side of the face did not move quite so freely as those on the right, but this was uncertain. There was certainly no definite paralysis of the facial muscles.

The tongue was markedly paralysed; it could only be protruded for a very short distance beyond the teeth; it was wrinkled, furrowed and studded with inequalities and projections which gave it a sort of hob-nailed appearance. It was the seat of constant fibrillary tremors. The tip when protruded was turned to the left. Both halves of the tongue, but especially the left, were thin and atrophied. This condition of the tongue was very remarkable. I have never seen anything like it in a child before. It exactly resembled the condition of the tongue in some cases of glosso-labio-laryngeal ('bulbar') paralysis. (See *Atlas of Clinical Medicine*, Plate XIII.)

When the child cried, the uvula was drawn symmetrically upwards in the middle line; on tickling the pharynx with the blunt end of a tuning-fork, no reflex contraction of the uvula or palate could be produced.

There seemed to be some paralysis of the pharynx.

When at rest, the vocal cords were placed somewhat closer together than normal; they were perfectly closed (adducted), but imperfectly separated (abducted). The abductor paralysis seemed to be more marked on the right than on the left side.

There were no disturbances of sensation either in the skin or organs of special sense.

The right pupil was a little larger than the left. The optic

March and the 1st of July—a period of more than three months—was *nil.* I would particularly note that notwithstanding the fact that the patient had been taking seven grains iodide of potassium three times a day for five or six weeks—and seven grains is a fairly large dose for a child of six—the headache was not relieved and the paralysis had increased rather than diminished.

At this visit also (July 1st), the mother showed me a round ulcer about the size of a half-crown on her arm (see Plate LXXXII. fig. 1). The ulcer was undoubtedly specific in character. It gave me the clue to the true nature of the case. There could be no doubt that the mother was suffering from tertiary syphilis.

I would here again observe that there had been nothing in the history which I had previously obtained to suggest syphilis. Further, the boy's appearance was in no way indicative of inherited syphilis. Nevertheless, it is certain that both the mother and the boy were the subjects of constitutional syphilis. The result of the treatment which we now adopted, the future progress of the case and the additional facts which were now elicited regarding the family history conclusively showed this.

The moment I saw the ulcer on the mother's arm I, of course, concluded that the intra-cranial lesion in the boy was probably syphilitic. A more minute enquiry into the family history confirmed this opinion, and the immediate disappearance of all the acute symptoms under more energetic anti-syphilitic treatment proved that it was correct

As I have already pointed out, the family consisted of nine children. The first five children are all alive and are all absolutely strong and healthy. Then there was a miscarriage; then two dead-born children; then a child, which died when it was three months old apparently from syphilis; and then our patient.

Now, that is a very striking history. There can be no doubt that after the birth of her fifth child the mother became affected with constitutional syphilis. The family history conclusively shows this; the fact is brought out in a very striking way in the following table:—

Tabular Statement of Family History.

1. A boy, now 22 years of age, very healthy.
2. „ „ 21 „ „
3. „ „ 19 „ „
4. „ „ 17 „ „
5. „ „ 15 „ „

Miscarriage at 3d Month.

6. A girl, born prematurely at 7th month; lived one week.
7. A girl, born prematurely between the 6th and 7th months; did not survive its birth.
8. A boy. He was delicate from his birth, and died when three months old from some pulmonary complaint; the doctor said he had a 'weak constitution'; he suffered from snuffles, and had some roughness and redness about his fingers, but (his mother says) no sores on the buttocks and no eruption on other parts of the body.
9. *The Patient.* Born at the full time. His mother states positively—and this is a very important point—that he was quite healthy during infancy. Careful cross-examination failed to elicit any evidence of congenital syphilis until the attack of influenza at the age of 4¾ years, when the headache, vomiting and other cerebral symptoms developed.

The subsequent progress of the case was as follows:—

As soon as I saw the ulcer on the mother's arm, I increased the dose of iodide of potassium from seven to ten grains three times a day, and ordered in addition a grain of grey powder night and morning. The mother was also put on iodide of potassium and mercury, and black-wash was applied to the ulcer.

The result in both cases was immediate improvement. In three weeks, the ulcer on the mother's arm, which had shown no indication of healing during the five weeks that it had been previously in existence, was completely healed. In a fortnight, the boy's headache was entirely relieved, and all the acute symptoms had disappeared. This satisfactory result must, I think, be chiefly attributed to the mercury rather than to the slightly increased dose of the iodide.

On *September 20th,* his mother stated that the boy had been completely free from headache for five or six weeks, that he had been looking well, eating well and feeling well. The paralysis was of course still present, but it was less marked; he could move his leg and arm more freely; and the tongue seemed less affected than it had been two months previously. He was ordered to continue the medicine.

On *December 14th,* it was noted:—The patient is very well; he has gained flesh and is now, his mother says, 'as fat as his skin can hold.' The paralysis of the arm and leg remains much *in statu quo*; the slight facial paralysis has cleared off, the tongue can be moved more freely; it is still wrinkled and markedly atrophied, and is still the seat of constant fibrillary twitchings.

On this day, the mother stated that she had not given the boy any medicine during the past month, for she had noticed that of late it (the iodide of potassium) had made his nose and eyes run. During the time that he suffered from headache it never, she says, affected him in this way.

On *February 14th,* 1894, when the patient was last seen, his condition was unchanged; his general health was excellent; the paralysis was much *in statu quo.*

On *October 24th,* 1894, the mother again consulted me at the Hospital on account of sore throat and ulceration of the palate. When asked how her son was she said, 'Oh! he died on the 4th of April.'

On further enquiry I ascertained that, after the last visit on February 14th, he had remained well until a fortnight before his death. He then began to complain of severe pain in the head, nape of the neck and spine (especially the upper part), became very feverish, but did not vomit. During the last week of his illness he took several epileptiform convulsions; he was insensible for two days before his death. This attack commenced without any obvious cause. Dr. Cowan Guthrie, who attended him, subsequently wrote me stating that the cause of death was cerebro-spinal meningitis, which apparently had its starting-point in the old lesion at the base of the brain. Dr. Guthrie regarded the last and fatal attack as a recurrence of the old head trouble.

I may add that on examining the throat of the mother I found a typical specific ulceration of the palate. It healed completely in the course of a few weeks, under a grain of grey powder and twenty grains of iodide of potassium three times a day.

Comments.—The case presents many points of interest. Let me briefly refer to some of them.

In the *first* place, it shows, if the mother's statement was correct—and I see no reason to doubt it—that a child may be the subject of inherited syphilis and may suffer from grave

tertiary lesions without manifesting any symptoms or signs of syphilis (snuffles, skin eruption, etc.) during infancy. It is of course quite possible that there may have been some slight infantile symptoms (coryza and skin eruption) which were not noticed.

Further, the case shows—and I have met with more than one other case of the same kind—that tertiary lesions due to congenital syphilis may develop in patients who present none of the characteristic physiognomic peculiarities indicative of congenital syphilis. This is only another way of restating the fact, that, when there are no infantile symptoms or when the infantile (secondary) symptoms are very slight, evidences of the syphilitic constitution are not stamped upon the physiognomy.

It is of course possible that had this boy lived to get his second set of teeth the central incisors might have been characteristically misshaped. But unless the permanent teeth had been misshaped, or interstitial keratitis had developed and left corneal opacities behind it, this patient, if he had lived to be an adult, would not have presented any external appearances suggestive of inherited syphilis. His face and head were normally shaped; his nose was not sunken; there were no linear scars at the angles of his mouth, and there was no choroiditis.

I will afterwards refer to another very interesting and striking case of the same kind.

In the *second* place, the case shows the great importance of carefully investigating all the details of the family history. If, when I first saw this child, I had obtained full information as to the family history, I should certainly have concluded that the intra-cranial tumour was probably syphilitic rather than tubercular.

In the *third* place, the case shows the importance, if one suspects the existence or the possible existence of syphilis in the child, of examining the parents and other members of the family; and *vice versâ*, if one suspects syphilis in the parents, of examining the children, in order to see whether they bear the specific stamp—whether there are any indications on the surface of the body of present or former syphilitic lesions.

In this case, the ulcer on the mother's arm cleared up the whole diagnosis. The photograph which is reproduced in Plate LXXXII., fig. 1, is an object lesson which will impress itself on the memory of the reader much more forcibly than any mere words can do.

In the *fourth* place, the case is a good illustration of the fact that tertiary lesions, especially gummatous lesions of the brain and its membranes, are apt to be developed after some depressing cause, illness, or injury, such as a blow on the head, a severe illness, overwork, worry—anything, in short, which disturbs the circulation in the brain and its membranes and produces cerebral congestion. In a previous article (see *Atlas*, vol. ii. page 65) I have emphasied this point. In this case, the patient enjoyed good health and presented no evidence of syphilis until his attack of influenza. He then began to suffer from headache and cerebral vomiting. Just before and during his attack of measles, the paralytic symptoms developed.

In the *fifth* place, the case shows in a very striking way the beneficial effect which mercury produces in many syphilitic lesions. The case is most instructive in this respect. The patient had been taking seven grains of iodide of potassium for several weeks without any distinct benefit. As soon as the syphilitic nature of the lesion was definitely diagnosed, the dose was increased to ten grains and mercury was prescribed. After this, he immediately improved; and within a fortnight, the headache was completely relieved. It is reasonable, I think, to conclude that this result was chiefly due to the mercury. I have seen several other cases of tertiary nerve syphilis in which mercury has produced a cure when iodide has failed. The more I see of syphilitic cases, the more I am impressed with the value and importance of mercury in their treatment. The beneficial effects of mercury are usually more marked in the primary and secondary than in the tertiary stages of the disease; but I repeat that there are many cases of tertiary syphilis in which mercury is most beneficial.

In the *sixth* place, this case shows—and this is a point of great importance which is too often forgotten—that although syphilitic lesions and the symptoms which are *directly* due to such lesions may be relieved and cured by means of anti-syphilitic treatment, the indirect results of the lesion and the symptoms which are due to those results will remain. In this case there was, I think, without doubt, a gumma pressing upon the left pyramidal tract and involving the hypoglossal nerves or the hypoglossal nerve nuclei. Now, such a lesion is apt to produce two different and distinct effects or results in the nerve structures which it implicates. In the *first* place, it may act as an irritative lesion. Headache, vomiting, localised epileptiform convulsions and double optic neuritis, are the results of this irritation or of the increased intra-cranial pressure which the lesion produces. In the *second* place, it may act as a destructive or destroying lesion. Paralysis and hemianopsia are some of the symptoms which may result from this destruction. These effects and results are very different. Under the administration of large doses of iodide of potassium or iodide of potassium and mercury, the gumma may be rapidly cleared away; the irritative effects which it is producing will then disappear, and the nerve tissues which are irritated will cease to discharge in a pathological manner, i.e. will functionate normally. But it is a very different thing when the gumma has produced destruction of tissue; for the removal of the gumma cannot restore nerve tissues which are destroyed to their previous healthy condition.

In this case, the headache disappeared with the disappearance of the gumma, but the paralysis remained. Syphilitic hemiplegia, as it is sometimes termed (provided of course that the paralysis is due to destruction of nerve tissue and is not merely post-epileptic in character) is no more curable by iodide of potassium and mercury than any other form of hemiplegia. Antisyphilitic treatment may remove the gumma or the syphilitic endarteritis, but it cannot restore the nerve tissues which are softened or destroyed. If the paralysis is to be recovered from, it must be the result of a slow and gradual restoration of the nerve structures which have been destroyed We have to trust to Nature rather than to iodide of potassium to effect this restoration.

In speaking of the two forms of pathological change in the nerve tissues which result from a cerebral gumma and the course which these two different forms of pathological change and the symptoms which they produce are apt to pursue, it must be remembered that the irritative symptoms do not always disappear with the removal of the gumma. It not unfrequently happens that the cicatrix which remains on the surface of the brain continues to act as a source of irrita-

tion, or that the habit to discharge pathologically and to produce convulsions continues. To cure the epilepsy in cases of this kind, one must cut out the cicatrix (i.e. remove the cause of irritation) or the portion of brain tissue which has acquired the habit of discharging in a pathological way. Had our patient lived, further improvement would, I think, in all probability have taken place; but in cases of this kind it is always difficult to predict the degree of improvement which will result. Some paralysis usually remains as a permanent condition. As a matter of practical experience, we know that a lesion (a hæmorrhage or a softening) which destroys the fibres of the great pyramidal tract, either in the internal capsule or in any part of its course through the pons Varolii, medulla oblongata, or spinal cord, usually results in the production of permanent hemiplegia. Even in young subjects, recovery is rarely complete. Had this boy lived, he would probably have continued to drag his leg, and he would most likely have had difficulty in performing the fine and more highly specialised movements of the fingers and hand. The paralysis of the tongue would probably have improved; but the subsequent behaviour of the paralysis of the tongue would have largely depended upon whether the nerve nuclei or the trunks of the hypoglossal nerves were involved by the lesion. A paralysis which is due to destruction of motor nerve cells (i.e. of the nerve nucleus) is usually permanent. In illustration, I need only mention the paralysis and atrophy which result from poliomyelitis anterior acuta, glosso-labio-laryngeal paralysis and progressive muscular atrophy.

But the paralysis and atrophy which result from a destruction of peripheral nerve fibres is usually recovered from provided, of course, that the lesion, the cause of the destruction, can be removed. There seems to be almost no limit to the power of restoration in the peripheral nerves. Witness the remarkable improvement and complete cure which occurs in so many cases of severe alcoholic neuritis. Degenerated fibres in the pyramidal tract are not so easily restored. This fact would seem to suggest that the motor nerve cells of the cerebral cortex do not exert such a powerful trophic influence upon the fibres of the pyramidal tract as that which the nerve cells of the anterior cornua of the spinal cord exert upon the fibres of the peripheral motor nerves.

Another point of interest in the case is this, that iodism was only produced after the headache had subsided. So long as the headache was severe, the iodide of potassium agreed well with the patient. It was only when the headache and other acute symptoms disappeared, in other words after the gummatous lesion was removed, that running of the eyes and nose was developed. This illustrates an important therapeutic fact, viz., that in those cases in which iodide of potassium disagrees with the patient it is (usually) unnecessary or contra-indicated; whereas in those cases in which the remedy is well borne, it is usually beneficial. The same statement applies to many other remedies.

This case, then, is an excellent example of a tertiary nerve lesion the result of congenital syphilis. Such lesions are undoubtedly rare. They are far more rare than gummatous lesions in adults who are the subjects of acquired syphilis.

Before concluding this article it may perhaps be well to refer to the whole subject of congenital syphilis in more detail.

SYSTEMATIC ACCOUNT OF CONGENITAL OR INHERITED SYPHILIS.

The infantile stage of the disease. — A child who inherits and actively manifests congenital syphilis, if born at the full time, is usually to all appearances healthy. In most cases, the symptoms of the disease do not show themselves until some weeks after birth. The infant then begins to suffer from coryza (snuffles), eruptions appear upon the skin, it loses colour, emaciates, and other symptoms to which I will presently refer in some detail may be developed.

In other cases, the child is manifestly diseased at the time of birth. In some cases, it is under-developed, shrivelled and emaciated. In cases of this kind, syphilitic infants look, as it is said, 'like little old men with skins too big for their bodies.'

In rare cases, the skin at the time of birth is covered with a copper-coloured macular or papular rash (see Plate LXXXII., fig. 2), more usually an eruption of pemphigus. In the vast majority of cases in which an eruption of pemphigus is present at the time of birth or is developed within the course of a few days after birth, the disease speedily proves fatal. The most frequent seats for this eruption are the soles and palms, but it may be distributed over the face and surface of the body generally. It has been much debated whether this eruption (*pemphigus neonatorum*) is a true syphilitic lesion or not; there can be no question that it is very rarely if ever present, at or soon after birth, except in infants who are the subjects of inherited syphilis. During the five years that I had medical charge of the Tynemouth Union Workhouse Hospital, I had an opportunity of seeing one well marked example of this kind and also examples of almost every other manifestation of congenital syphilis. In some cases, the child suffers immediately after birth from coryza and the cry is hoarse.

Syphilis is a frequent cause of miscarriages, dead-births and premature births. The family history in cases such as that which I have previously related conclusively shows this. In commenting upon that case, I have emphasised the importance, in cases of suspected congenital syphilis, of making a detailed and minute enquiry into the family history—the occurrence of miscarriages, premature births, dead-born children, etc.

In many of the cases in which the child is dead-born or in which miscarriages occur, the placenta is diseased. In some cases, the miscarriage occurs during the early months of pregnancy; in others, the child is dead-born at a later period. In many of the cases in which the child is dead-born, it is under-developed and semi-macerated, its skin decomposed and peeling; in these cases the liquor amnii is usually dark-coloured and blood-stained.

In most of the cases in which a syphilitic child is born alive but prematurely, it dies within a few days after birth. In some of these cases, the bones have been found to be diseased; in others, but this is very rare, the lungs are affected with white pneumonia—a condition to which I have already referred in the article on acquired syphilis (see *Atlas*, vol. ii. page 61).

In those cases in which a syphilitic child survives when born prematurely, the usual symptoms characteristic of the infantile form of the disease are subsequently developed. Let me refer to these symptoms in more detail.

I have already stated that, in the great majority of cases, children who actively inherit syphilis and who are born at the full time do not present any distinct evidences of the disease at the time of birth. In some cases, it is true, they are under-developed, emaciated, miserable-looking children; but in many cases they are plump and well-nourished.

With rare exceptions, the characteristic symptoms appear within the first two or three months after birth.[1] In most cases, within the course of two or three weeks, an erythematous eruption appears on the skin and it is noticed that the child has difficulty in breathing through its nose. This coryza is a highly characteristic symptom. At first the discharge from the nose is thin and watery; in the course of a short time it becomes thicker and it may be sanious; the nose becomes choked and blocked with scabs and crusts, and the difficulty in breathing is consequently aggravated. In popular language, the child is now said to be suffering from 'snuffles.' The impediment to the respiration through the nose prevents its sucking properly; it cannot keep hold of the breast and draw the nourishment in the natural way; its nutrition consequently suffers; it rapidly emaciates and becomes wizened and old-looking. It is fretful and peevish, and its cry is rough and hoarse in consequence of the presence of syphilitic lesions (congestion and swelling, perhaps sometimes mucous patches, probably very rarely ulceration) in the laryngeal mucous membrane.

The skin eruptions are usually at first macular (erythema or roseola) or papular; later, vesicles, pustules, scabs, crusts, cracks and ulcerations may be developed.

The eruptions may be distributed over the whole surface of the body, but they usually first appear on the abdomen, lower part of the chest, face and inner side of the thighs and arms. When well-developed, the eruptive lesions are usually most marked around the mouth, nose and anus and over the nates and scrotum; this is no doubt due to local irritation. Unless great attention is paid to cleanliness, the urine and fæces are apt, even in healthy children, to produce an excoriated and eczematous condition of the buttocks and scrotum.

The eruption usually at first consists of round or oval-shaped patches about the size of a threepenny piece or a sixpence. The margins of the patches of eruption are usually well defined. In the course of a short time, the individual patches of eruption tend to coalesce and run one into the other, so that ultimately large portions of the skin may be covered with the rash. The macular and papular rashes are usually of a bright red, reddish-brown or raw-ham colour. When the buttocks and scrotum are extensively covered with the rash, the skin often has a glazed, varnished appearance and a leathery feel. The skin at the seat of the eruption and especially round the margins of the patches often desquamates in the form of branny scales or larger flakes. The skin at the seat of the eruption often becomes moist and excoriated.

The palms and soles are often covered with a diffuse redness and studded with scaly or desquamating patches; on the palms and soles the eruption is usually scaly. The finger tips are in many cases red and inflamed and the skin surrounding the red areas is in many cases partly detached and peeling. The nails are in some cases compressed laterally or affected with onychia. The eyebrows in some cases become covered with scabs.

Deeper ulcerations and more extensive destructions of the skin are in some cases produced in the position of the eruptive lesions.

Mucous patches, cracks (rhagades) and ulcers develop about the mouth, anus and nose, and on the tongue and buccal mucous membrane. On moist surfaces such as the interior of the mouth the mucous patches are usually ulcerated. The radiating cicatrices which result from the ulcers and cracks at the angles of the mouth in many cases persist and form an important diagnostic mark in after-life. The inflammatory lesions and ulcerations in the nose often extend to the deeper parts; the bone may be destroyed and the bridge of the nose may become permanently depressed. A depressed sunken nose, broad at the tip and with little or no bridge, is, in after life, highly characteristic of congenital syphilis. Such a condition shows that the nose was severely affected during the infantile (secondary) stage of the disease. In some cases, the inflammatory lesions in the nose extend along the Eustachian tubes to the ear. Permanent deafness may be the result; but it is a rare result during this, the infantile (secondary), stage of the disease.

In consequence, partly of the rapidly advancing disease which is widely distributed through the tissues of the body and of the anæmia and cachexia which the syphilis produces, and partly of the difficulty in sucking and the resulting inanition, the nutrition is gravely impaired; the child becomes thin, wizened, pinched and old looking.

The hair may fall out or become thin as in the acquired form of the disease. In some cases, the lymphatic glands beneath the jaw and in the neck are in some slight degree enlarged, but the adenopathy is much less marked and characteristic than in the acquired syphilis of adults.

If the child survives, iritis may be developed; it rarely occurs before the fifth or sixth month, usually later than this.

In many cases, the liver and spleen become enlarged. From a diagnostic point of view, the enlargement of the spleen is more important than that of the liver, for the liver is naturally large in infants. In many cases, the bones are affected by a condition which has been termed syphilitic osteo-chondritis. The bone at the junction of the diaphysis and the epiphysis is enlarged; the cartilage becomes greatly thickened, friable and opaque as if it were encrusted with mortar; osteophytes may be developed round the thickened part. The head of the bone may be separated from the shaft. These bone changes, which according to some observers are due to a gummatous lesion, may, as I have already remarked, be present in dead-born fœtuses, the subjects of inherited syphilis. When the bone and joint lesions are severe, a condition of complete imobility of the affected limbs and apparent paralysis (syphilitic pseudo-paralysis) is sometimes present.

[1] In 158 cases analysed by Diday (*Infantile Syphilis*, New Sydenham Society's Translation, page 101) the date of appearance of the symptoms was as follows:—

Before the completion of one month after birth	in 86
Before the completion of two months	in 45
Before the completion of three months	in 15
At four months	in 7
At five months	in 1
At six months	in 1
At eight months	in 1
At one year	in 1
At two years	in 1

The severity of the symptoms is very variable in different cases. In this respect, infantile syphilis exactly corresponds to the secondary stage of acquired syphilis in the adult.

In many cases, the disease is so severe that the child dies within the course of a few weeks or months; a fatal issue is especially apt to occur in those cases in which the child is prematurely born and in severe cases which are allowed to run their course without treatment; cases which are actively treated in their initial stages with mercury very rarely prove fatal. In others, the symptoms are so slight that they may easily escape detection. Between these two extremes there are all degrees of difference.

In those cases in which the disease does not prove fatal, the symptoms for the most part disappear within the course of twelve months and this occurs whether the child is treated or not; but relapses are apt to occur.

In those cases in which the infantile symptoms are slight, the child may grow up and develop in the ordinary manner without presenting any further symptoms or signs of the disease. In cases of this kind, there may be nothing in the appearance of the child when it reaches the age of puberty to show that it is the subject of inherited syphilis.

In the more severe cases, the effects of the disease may be permanently stamped upon the physiognomy.

But it is important to remember that in both classes of cases, in the slight cases as well as in the severe ones, further indications of the disease may be subsequently developed—the permanent teeth (central incisors of the upper jaw) may be misshaped, interstitial keratitis may develop, gummatous lesions in the palate and internal organs and other tertiary manifestations of the disease may occur during later childhood, about the age of puberty or even during early adult life.

It is probable that the more severe the infantile (secondary) stage of the disease, the greater is the tendency to remote and tertiary manifestations, but to this rule there are undoubtedly many exceptions The case of gumma of the medulla oblongata which I have described in detail is a good example in point. I will refer to other cases of a similar kind later.

Congenital syphilis differs from the acquired disease in this important fact, that there is no primary sore or lesion to be detected upon the surface of the body. A child who is the subject of inherited syphilis is inoculated with the syphilitic virus, either at the period of conception (i.e. it is developed from a syphilitic sperm-cell or a syphilitic germ-cell) or from the blood of its syphilitic mother during intra-uterine life. The symptoms which it manifests soon after birth are for the most part secondary symptoms; they correspond more or less closely to the secondary symptoms of acquired syphilis in the adult. It should, however, be stated that during infancy, tertiary lesions are not infrequently developed. It would appear that precocious tertiary lesions are more apt to occur in the congenital than the acquired form of syphilis. In the syphilitic infant, the secondary and tertiary stages are more often mixed up so to speak than in the adult.

In the congenital as in the acquired form of syphilis, tertiary symptoms may be developed at a later period; and, as I have already remarked, when the individual attains adult age the effects of the infantile stage of the disease may be indelibly stamped upon the physiognomy.

The physiognomic appearances indicative of congenital syphilis.—The facial and other characteristic symptoms and signs of congenital syphilis in later life are the result partly of the alterations produced during the infantile (secondary) stage of the disease, and partly of later developments (malformations of the teeth, interstitial keratitis) to which I must now more particularly refer.

In those cases in which the infantile stage of the disease is severe, the development of the whole body is apt to be interfered with. The subjects of hereditary syphilis are often stunted and under-developed; the sexual development is in many cases retarded; at twenty years of age, they may look like children. This dwarfing of the body is admirably seen in the patient who is represented in Plates LXXXI. and LXXXII., fig 3.

In characteristic cases, the forehead is square, the frontal eminences prominent, the nose short and squat, sunken and depressed, the bridge broad and flat, the complexion pale or of an earthy tint, the skin thick, coarse and as it has been termed 'pasty,' the teeth malformed in a way which I will presently describe in detail, the irides of a steel-grey colour, and the corneæ more or less cloudy and opaque from the remains of interstitial keratitis. In some cases, linear cicatrices are seen about the angles of the mouth, and small pits and depressed cicatrices, the results of the eruptive lesions are present on the face or other parts of the surface of the body In many cases, the sight is imperfect either as the result of scars on the corneæ, the result of interstitial keratitis (see Plate LXXX and Plate LXXXII, fig 5), or of changes in the fundus (choroido-retinitis, etc) Mr Hutchinson has pointed out that in some cases the patients have a slight tendency to frowning, consequent, he thinks, on prolonged intolerance of light during the period of keratitis.

Most of these appearances are remarkably well seen in Plate LXXX. The only respect in which that case is not quite typical is the bright colouration of the face. This has been somewhat exaggerated by the artist, but the complexion in reality was markedly high-coloured—very different from the pale, earthy tint which is usually associated with the other characteristic features which have just been described.

In those cases in which the secondary symptoms are slight and in which the infantile stage of the disease is carefully treated, the development of the body at the time of puberty may be in no way interfered with.

Let me now refer in more detail to some of the points which have been incidentally alluded to in the foregoing description.

The condition of the teeth.—Mr. Jonathan Hutchinson was the first to show that the teeth of patients who are affected with congenital syphilis are in many cases malformed. The characteristic alterations affect the central incisors of the upper jaw; they are dwarfed, short and narrow at their free ends (screw-driver shaped), and their free edges are scooped out by a single central cleft (see Plate LXXX. and Plate LXXXII., fig. 4). In many cases, they are widely separated from one another at their points of insertion into the gum, but converge towards their free ends. Mr. Hutchinson has specially insisted upon the fact that, if errors in diagnosis are to be avoided, the attention of the observer should be concentrated upon the condition of the central incisors in the upper jaw or as he terms them 'the test teeth'; they are the only ones the condition of which is positively characteristic; the condition of the other teeth may afford corroborative evidence, but is not to be relied upon. It is important to remember that these characteristic alterations which are of so much import-

ance for diagnosis, affect the permanent set of teeth alone. The first set of teeth may be late in appearing; they usually decay prematurely, but their state is in no way characteristic.

Although the teeth are characteristically malformed in the majority of cases of (severe) inherited syphilis, the malformation is by no means constant. Mr. Hutchinson has pointed out that in those cases in which the nose suffers, the teeth often escape. In some exceptional cases, in which gummatous lesions such as ulcerations of the palate are developed about the age of puberty or during early adult life, the teeth may be quite normally shaped and there may be absolutely no indications in the physiognomy suggestive of congenital syphilis. I will presently refer to an illustrative case. (See Plate LXXXIII., figs. 1 and 2.)

Interstitial keratitis.—This is a highly characteristic result of inherited syphilis; it is usually developed between the eighth and the fifteenth years, but may occur earlier or later; it is more common in girls than in boys. It begins with a cloudiness of the substance of the cornea, some ciliary congestion and irritability. The opacity and cloudiness of the cornea gradually increase until the cornea looks like a piece of ground glass. One eye is first affected, but in the course of a few weeks the other usually becomes attacked. According to Mr. Hutchinson, the condition is always in the end symmetrical, although in rare cases the interval between the attacks in the two eyes may extend to several years. When the keratitis is at its height, the sight may be almost entirely abolished. After this stage is reached, marked improvement usually occurs; in many cases the corneal opacity clears up so satisfactorily that very slight impairment of vision remains as a permanent condition. In typical cases of syphilitic keratitis (see Plates LXXX. and LXXXII., fig. 5) the teeth are usually misshaped and the other physiognomic appearances characteristic of the disease are often present. With reference to this point, Mr. James Dixon says:—'We may meet with some syphilitic keratitis in patients with healthy physiognomy and deformed teeth, or, still more rarely, in those with faultless teeth and the syphilitic cast of features; but to find the true form of keratitis in connection with both good teeth and good complexion is, I think, next to impossible.'[1]

The keratitis is sometimes associated with iritis, scleritis, or choroiditis. In some cases of congenital syphilis, a condition resembling retinitis pigmentosa is developed.

Deafness from an affection of the ear.—In some cases of congenital syphilis, the patient becomes deaf from an affection of both ears. The deafness is rarely developed before the age of puberty; the onset is in most cases gradual. The deafness seems to depend upon an affection of the auditory nerve or its nerve terminations. In some cases, the deafness is attended at its onset or during its development with noises in the ears, but there is no otorrhœa, and there are no external evidences of ear disease. The condition presents different degrees of severity. In some cases, it is recovered from; in others, it goes on to complete and permanent deafness. In some cases, as in that represented in Plate LXXXIII., fig. 3, the deafness is associated with other cerebral lesions.

Affection of the bones.—Periosteal thickenings and inflammations and recurring attacks of synovitis are in some cases developed. The synovitis is particularly apt to affect the knee-joints and is usually symmetrical. In the case which is represented in Plate LXXXII., fig 6, the tibiæ are characteristically affected; there is an overgrowth of bone in length as well as in thickness. In that case, the condition was attended with a considerable degree of pain, but in many cases pain is much less prominent than one would expect. Occasionally but rarely, the periostitis goes on to suppuration and necrosis. The bones of the fingers are in some cases affected (syphilitic dactylitis). During the infantile (secondary) stage of the disease, the bones often present characteristic changes. The humerus, radius, ulna, femur and tibia are most frequently affected. The alteration consists of a thickening between the diaphysis and the epiphysis. New bone (osteophytes) is frequently produced. Nodular thickenings around the anterior fontanelle are highly characteristic.

Ulceration of the palate.—In some cases, destructive ulcerations of the palate develop. In many cases, these ulcerations of the palate are associated with disease of the nose and pharynx. In cases of this kind, the physiognomy is usually typical and characteristic (see Plates LXXX. and LXXXIII., figs. 4 and 5). The uvula may be completely ulcerated away, and the uvula or pillars of the fauces may become adherent to the posterior wall of the pharynx, so that a narrow opening merely remains between the mouth and the throat (see Plate LXXXIII, fig. 5). In cases of this description, there may be considerable difficulty in swallowing.

In some cases of congenital syphilis a destructive ulceration of the soft or hard palate is the only evidence of the disease. A striking case of this kind is detailed below and is represented in Plate LXXXIII., figs. 1 and 2. Mr. Hutchinson states that acute destructive ulceration of the palate in a young person is in itself an almost conclusive proof of inherited syphilis, and that the absence of keratitis and malformed teeth does not in cases of this kind negative the diagnosis. The case to which I have just referred entirely confirms this statement.

Ulcerations of the skin.—Extensive ulcerations, the result of gummatous lesions, are sometimes developed in the skin In the case which is represented in Plate LXXXIII., fig. 6, the side of th[illegible]nd ear were extensively affected. In the case which is [illegible]ed in Plate LXXXIII., figs. 4 and 5, numerous cicatrices were present on both sides of the neck. They appeared to be the result of scrofulous lesions in a highly (congenital) syphilitic subject. The cicatrices were smooth on the surface, raised and thickened. In short, a keloid condition had developed in the cicatrices.

Visceral and nervous lesions.—Gummata and other tertiary lesions are occasionally developed in the internal viscera and nerve centres. They are far less common than in the acquired form of the disease; but they probably occur more frequently than is generally allowed.

In some cases, these tertiary symptoms are developed during infancy in association with or soon after the secondary symptoms. In other cases, they occur during early childhood (see Plate LXXXII., fig. 1). In other cases again, they may not develop until the age of puberty or early adult life.

I have previously referred to the enlargements of the liver and spleen which are of frequent occurrence during the infantile (secondary) stage of the disease. Similar changes may also occur in later childhood or about the age of puberty. In some of these cases, the enlargement of the liver appears to be due to a cellular proliferation diffused throughout the organ; in others, to waxy (amyloid) disease. The amyloid degenera-

[1] Holmes' *System of Surgery*, American Edition, page 71.

tion may affect the liver, spleen, kidney and intestine. I remember a few years ago making a post-mortem examination in a typical case of this kind—extensive amyloid degeneration in a young woman whose features were stamped with congenital syphilis. In the case which is represented in Plate LXXXII., fig. 6, the liver and intestines appeared to be 'waxy.'

It is probable, I think, that cirrhosis of the kidney in young persons is sometimes the result of congenital syphilis. I have examined post-mostem at least one case in which a cirrhotic condition of the kidney appeared to me to be due to this cause.

Occasionally gummatous enlargement of the testicle occurs.

In very rare cases, locomotor ataxia develops in childhood or youth; in all of the cases of this kind which have been reported (cases of Friedreich's ataxia must of course be carefully excluded) the patients, so far as I know, have been the subjects of inherited syphilis.

Occasionally, but very rarely, a condition of meningo-cerebritis, associated with symptoms of gradually progressive dementia, the result of congenital syphilis, is developed in later childhood or youth. General paralysis of the insane in young subjects (but it is a very rare condition), seems always to be the result of syphilis; and, since acquired syphilis is extremely rare in childhood, it is almost always due to the congenital form of the disease. In some cases, which are classed as general paralysis during life, the meningeal inflammation is much more marked than in the general paralysis of adults. A case which seemed to be of this nature, but which was complicated with epilepsy, is briefly recorded below.

In rare cases of congenital syphilis, the mental development is interfered with and the patients are idiotic. In these rare cases of syphilitic idiocy, the defective brain development is probably due to a diffuse syphilitic meningitis or cortico-meningitis in early life. In one well-marked case of this kind which recently came under my observation, the patient was blind from optic atrophy and choroido-retinitis. The facts of that case are briefly as follows:—

Case of syphilitic idiocy.—J. H., aged 7, was seen with Dr. Butchart on 30th March, 1894.

Previous History.—The patient is the first child of a family of five; she was born at the full time, ten months after marriage; her birth was not attended with any special difficulty; instruments were not used. Soon after birth, a brownish eruption appeared on the skin; it was most marked about the buttocks. She also suffered from snuffles. When a month or six weeks old, the left arm became paralysed. A month after this, she had a serious illness during which she had two epileptiform convulsions and was unconscious for some time. There was no fever and no vomiting. After this illness she lost her sight. Since this illness she has occasionally had attacks of vomiting and diarrhœa. Every now and again she takes crying fits which last the whole day; they used to be very frequent, but during the last three years there have only been two.

Family History.—The mother was married for ten months before the child was born. There have been no miscarriages.

There have been five children, viz.:—

1. The patient, aged 7.
2. Child aged 5; quite healthy.
3. Child died at the age of 9 months from, her mother says, constipation.
4. Child died at the age of 4 weeks from erysipelas.
5. Child aged 3 months; healthy.

Present Condition.—The patient is idiotic. She is unable to stand or creep. She seems to be quite blind. Her mother says that she thinks the patient can understand a few things which are said to her, but this seems very doubtful. She is unable to make any intelligible articulate sound.

The head is large and the physiognomy characteristic of congenital syphilis. The nose is sunken, the forehead square, the frontal eminences prominent. There are no teeth in the upper jaw. The pupils hardly respond at all to light. The optic discs are atrophied and the ophthalmoscope shows evidences of past choroiditis; it is difficult, however, to be sure of the exact condition of the fundus, for the patient keeps rolling the eyes constantly from side to side.

Remarks.—There can be no doubt that this patient is the subject of congenital syphilis. The idiocy is apparently the result of the brain lesion, the exact nature of which is doubtful, which occurred when she was about three months old.

In rare cases, a condition of complete ophthalmoplegia seems to be the result of inherited syphilis. In a previous article (*Atlas*, vol. i. page 122), I have described a characteristic case of this kind. In that case, a typical syphilitic dactylitis was also present.

It is of great importance to remember that many of the tertiary lesions to which I have just referred may be developed during later childhood, youth, or early adult life, and that in some of these cases, although the nature of the symptoms, the family history, collateral circumstances and the effects of treatment show without doubt that the lesion is syphilitic, the infantile (secondary) symptoms were very slight or, so far as can be ascertained, absent altogether. It is probable that in many of the cases of this kind in which a history of infantile symptoms cannot be elicited, some symptoms were actually present but were so slight that they escaped the attention of the mother or nurse. With reference to this point Mr. Hutchinson says:—

'The symptoms which usually betray the existence of syphilis in an infant may vary exceedingly in severity. In turn each one of those most common may be absent. There may be no snuffles, no eruption, no wasting, no soreness of the mouth. All authorities will admit that the group is often incomplete, and that whether complete or incomplete, it may be very faintly marked. Some, however, make it an important point to assert that there are no cases in which infantile symptoms are wholly absent. Positive proof that there are such it is exceedingly difficult, if not impossible, to give, for the reply may always be made that the infant was not sufficiently well watched. That there are many in whom, for all practical purposes, infantile symptoms are omitted, I have not the slightest doubt. I have seen many cases of keratitis at puberty or of bone or throat affections of undoubted character, and with the clear history of parental disease, in which nothing whatever had been ever observed in infancy. In some of these the entire absence of the usual marks of the disease in physiognomy, teeth, etc., quite bore out the parents' statement. I have seen many times a well-developed nose with a narrow bridge, a well-formed forehead, and good complexion in conjunction with keratitis of the most definite kind, and with corroborative facts of the clearest nature. Sometimes the teeth in such cases may be typically malformed, but this is rare. We may probably take it as certain, that when the bridge of the nose remains narrow no material degree of snuffles was ever present, and that if the complexion is good there was no rash on the face. The definiteness of the several marks by which the diathesis is recognised at puberty, is always in ratio with the severity of the disease in infancy.

'For practical purposes, then, we must admit that a taint of inherited syphilis may remain latent until at, or even considerably after, the age of puberty, it may manifest itself by a severe attack of interstitial keratitis, by deafness, nodes, lupus (specific), or ulceration of the palate. In saying this I am not speaking solely from observation of the children of the poor, who may be supposed to be sometimes negligent in observation, and apt to forget what has happened to their children. Some of those who illustrated the facts which I now describe were the offspring of most intelligent and observant mothers, and had also been more or less constantly under the notice of the family surgeon. In some instances one or two children in the family had suffered both in infancy and afterwards, whilst another who had shown nothing in

childhood yet displayed the usual conditions at adolescent periods.'[1]

In the case which is represented in Plate LXXXIII., figs. 1 and 2, infantile symptoms were said to have been absent, the physiognomy was in no way suggestive, but a typical syphilitic ulceration of the palate was present. The details are as follows:—

The patient, a well-grown lad aged 16½, was seen at the Edinburgh Royal Infirmary on 3rd April, 1894. He had suffered for three years from his throat. On examination, a round perforation was found in the soft palate (see Plate LXXXIII., fig. 2); the edges of the ulcerated aperture were ragged; it was undoubtedly syphilitic. The patient was well developed; his upper central incisors were in no way misshaped; the physiognomy was not in the least suggestive of congenital syphilis; there had been no keratitis. The patient had had a glandular abscess in the neck a few years previously; but he had otherwise been quite healthy. His mother stated definitely and positively that he was quite healthy as an infant and had not suffered from any skin eruption or snuffles.

The ulcer healed rapidly under iodide of potassium and mercury.

That the ulcer was syphilitic was clearly proved by:—(1) the nature of the throat lesion; (2) the immediate benefit and rapid cure which resulted from antisyphilitic treatment; (3) the family history and the condition of the patient's sister.

The family history was as follows:—The father, aged 36, was a delicate man (the exact cause of his delicacy was not ascertained). The mother, aged 38, had suffered from sore throat and loss of hair when the patient, the eldest child of a family of eight, was born. The ages of the children were:—

1. Patient, aged 16½. Healthy as an infant. At the age of 7½ years he suffered from a glandular abscess in the neck. At the age of 13½ he began to suffer from sore throat; it continued for three years and produced extensive destruction of the palate; the ulcer rapidly healed under antisyphilitic remedies. Teeth well formed; no physiognomic appearances suggestive of congenital syphilis (see Plate LXXXIII., fig. 1).

2. Girl, aged 14½; seen at the Edinburgh Royal Infirmary, April 3rd, 1894. She was delicate as an infant; troubled with snuffles and always bothered with her nose; had a tender skin as a young child; suffered from a sore bottom; for six months suffered from her eyes; at the age of seven years, began to take epileptic fits; they have continued since. Patient never was very bright, but during the past year her mental condition has greatly deteriorated; she is now in a condition of chronic dementia; a few months ago she began to lose her hearing and is now almost completely deaf. Her nose is sunken and her physiognomy characteristic of inherited syphilis (see Plate LXXXIII., fig. 3); the central incisors in the upper jaw are characteristically misshaped; there are scars on the corneæ and evidences in the fundus of choroiditis.

3. Boy; was found dead in bed when five months old; his mother says that he was a 'delicate' infant.

4. Girl, aged 11; always ailing as an infant; now has weak eyes. This patient was not seen.

5. Boy, aged 9; healthy.

6. Boy, died a few months after birth.

7. Boy, aged 5; very 'delicate' as a child; had a 'tender skin,' but did not suffer from snuffles.

8. Boy, aged 4; always quite healthy.

This case fully confirms Mr. Hutchinson's statement that in cases of ulcerating gumma of the palate in young persons, the teeth are seldom or never typical and there is often no keratitis.

In his work on syphilis, (page 337) Mr. Hutchinson has recorded a case of gumma of the palate in a youth of remarkably good development and without the slightest indication of the syphilitic diathesis, but in which the history clearly showed that the patient was the subject of congenital syphilis. In commenting on this case he says, 'The almost absolute absence of infantile ailments explains no doubt the absence of peculiarities in physiognomy and teeth. In some cases, there may be absolutely no evidence of the syphilitic taint until the outbreak of keratitis.

In rare cases, a condition of recurring iritis and iridocyclitis is developed in persons affected with congenital syphilis. In a case which was sent to me a short time ago by Dr. Stewart of Leith, the patient was a tall, well-grown young woman; her teeth were characteristically misshaped; she suffered from interstitial keratitis, iritis and iridocyclitis and very severe nocturnal headaches; a suppurating gumma was present in the region of the right tonsil.

Diagnosis.—The diagnosis of congenital syphilis is sometimes very easy, at others most difficult.

We have seen that the inherited form of syphilis may present both a secondary and a tertiary stage; that the secondary stage rarely continues longer than twelve months; and that the tertiary symptoms may be developed at any time after this period until early adult life or perhaps even later.

In well-marked and typical cases, there is no difficulty in coming to a conclusion as to the nature of the disease, during the infantile (secondary) stage of the disease. The emaciated, ill-nourished, anæmic condition of the child, the coryza and snuffles, the rough husky cry and the characteristic skin eruptions of a raw-ham colour are quite distinctive. The polymorphous character of the eruption is in many cases a diagnostic point of the greatest importance.

In slight cases, in which the only symptom is perhaps a doubtful skin eruption or a doubtful skin eruption with a slight coryza, the diagnosis may be very difficult. In such cases, the syphilitic nature of the condition is often proved by the therapeutic test—the rapid improvement and complete disappearance of the symptoms under the administration of mercury. I remember when in general practice getting great credit in a case of this kind. It had resisted simple remedies prescribed by a brother practitioner, but rapidly disappeared under the administration of mercury. In doubtful cases, the father should be questioned as to the existence of syphilis before marriage and the family history should be most carefully investigated. The importance of this point is very clearly shown in the case which forms the text of these remarks. The facts that there have been a series of miscarriages or premature births and that other children have died in early infancy are highly suggestive. The fact that others of the children have suffered from snuffles and skin eruptions during early infancy is still more important. The parents and the surviving children should always be carefully examined with the object of determining whether they present any external evidences of present or former syphilis; and it is unnecessary to say that the opinion of the ordinary medical attendant should, if possible, be obtained as to the previous health of the family and especially as to the occurrence during infancy of any symptoms or signs of syphilis in any of the children. In doubtful cases a knowledge of the kind of life which the father was in the habit of leading before marriage may throw light upon the case. But whether there is or is not reason to suppose that the father has had syphilis, it is eminently advisable in cases of this kind to try the effect of small doses of mercury.

After the secondary period is passed, the recognition of congenital syphilis is in some cases easy, in others most difficult.

When the characteristic physiognomic appearances (the square forehead, prominent frontal eminences, sunken nose, pale complexion, notched teeth, opacities of the cornea, scars

[1] *Syphilis* by Jonathan Hutchinson, F.R.S., LL.D., page 413.

about the mouth) are well marked, there is of course no difficulty whatever in saying that the patient is the subject of syphilis and has in all probability inherited the disease.[1]

When internal lesions, which from their nature may be specific, develop either in later childhood or during early adult life in patients who are stamped by such characteristic signs of inherited syphilis, it is reasonable to conclude that they are probably syphilitic.

But in some cases, the physiognomy is not characteristic. In such cases, the condition of the teeth and of the corneæ is of great importance. Typically notched teeth and interstitial keratitis are pathognomonic.

In rare cases, tertiary lesions are, as I have already pointed out, developed in patients who present absolutely no signs of inherited syphilis. Under such circumstances, the diagnosis can only be based upon:—(1) the nature of the symptoms and lesions which the patient exhibits; (2) the family history; (3) the condition of the parents and other children; and (4) the effects of treatment.

An acute destructive ulceration of the palate, as I have already remarked, in a young person, whether there are any other symptoms or signs of syphilis or not, is probably always syphilitic. A symmetrical synovitis of the knee-joints or a non-suppurative periostitis with elongation of the tibiæ, is highly suggestive of inherited syphilis. Ophthalmoplegia externa is also suggestive of a syphilitic lesion, but it may doubtless be due to other conditions, such for example as a scrofulous tumour at the top of the pons or in the region of the corpora quadrigemina. General paralysis of the insane and locomotor ataxia (the ordinary form of tabes, not Friedreich's ataxia) which, as I have already stated, are very rare conditions in young subjects, are probably always due to syphilis. Waxy (amyloid) disease in a young person, who is not suffering from lung disease and who has not suffered from prolonged suppuration or acquired syphilis, is also suggestive. The presence of a uniform, hard, non-painful enlargement of the liver is, under such circumstances, suggestive of amyloid degeneration due to congenital syphilis. I have already stated that I am disposed to think that cirrhosis of the kidney in young persons, provided that alcohol can be excluded, is suggestive and suspicious of congenital syphilis.

Prognosis.—It is impossible to lay down any general rule of prognosis applicable to all cases of congenital syphilis. Each case must be judged on its own merits, for different cases present, as we have seen, very different degrees of severity. Whether the child is born prematurely or at full time, the severity of the attack, the exact nature of the symptoms and lesions, the period of the disease at which the treatment is commenced and the effects of treatment are, for the purpose of prognosis, the most important points.

Speaking generally, it may be emphatically stated that inherited syphilis is a very grave disease. It is a frequent cause of miscarriage, of death *in utero* and of premature births. Most of the children who are born alive prematurely, as the result of congenital syphilis, die soon after birth.

In severe cases in which the disease is allowed to run its course without treatment infantile syphilis is often fatal. In the less severe cases, early mercurial treatment is attended with rapid improvement, and in the more severe cases, the prolonged use of mercury and careful feeding and nursing, provided that there are no grave internal lesions, is, in my experience, almost always successful in tiding the patient over the attack.

The prognosis of tertiary lesions depends upon their nature and severity. An interstitial keratitis, even when severe, usually clears up to a very large extent under appropriate treatment and leaves comparatively little, if any, dimness of vision. Ulcerations of the palate generally heal with great rapidity under antisyphilitic remedies. The same statement may be applied to all the external and many of the internal lesions. No better illustration can be given than the case of ophthalmoplegia externa which I have reported in a previous volume of this work. Bilateral deafness when complete is, in the experience of Mr. Jonathan Hutchinson to whom we are indebted for pointing out the syphilitic nature of the condition, usually permanent and incurable.

A gumma in the region of the medulla oblongata, such as was present in the case which I have recorded in the preceding pages, is necessarily a very dangerous lesion. The result in that case shows that even if the symptoms clear up under treatment, a relapse may occur and the disease may prove fatal.

Idiocy, general paralysis of the insane and locomotor ataxia, which fortunately are extremely rare results of congenital syphilis, are incurable.

Treatment.—The treatment is essentially the same as for the acquired syphilis in the adult. The beneficial influence of mercury is most striking, more particularly during the infantile (secondary) stage of the disease. The drug may be given internally in the form of grey powder, a grain two or three times a day, or applied externally in the form of inunction; an effective method is to smear mercurial ointment on the binder which the child wears. After the more severe symptoms have subsided, the remedy should be continued in small doses, the effects being of course carefully watched, for several weeks or months.

The mucous patches, ulcers and sores should be dusted with calomel or iodoform, or painted with nitrate of silver. The nose should be kept clear of crusts and brushed out with blackwash, weak perchloride solution, boracic solution, a solution of menthol in olive oil (10°/₀), etc.

During the tertiary stage, iodide of potassium should be combined with the mercury. In the case of gumma of the medulla oblongata which I have recorded in the preceding pages, no improvement resulted until mercury was added to the iodide; immediate improvement then took place. I have noticed exactly the same thing in other cases; but in many cases the tertiary lesions completely clear up under the iodide alone. The case of ophthalmoplegia to which I have already more than once referred is a good example in point.

Precocious locomotor ataxia and precocious general paralysis of the insane do not appear to be influenced by antisyphilitic remedies. Their prognosis is no more favourable than the corresponding affections in the adult. They are indirect, not direct results of the syphilitic poison.

It is unnecessary to say that children who are suffering from inherited syphilis should be carefully fed and nursed; great care should be taken to keep them clean and to prevent any external irritation.

And here I would wish to emphatically point out that during

[1] In rare cases, a child may acquire syphilis during infancy. The possibility of this must of course be taken into account.

the infantile period the disease is highly infectious and may be readily communicated to healthy people; indeed many of the best authorities (Diday and Fournier, for example) maintain that the lesions of congenital syphilis are far more contagious than the corresponding lesions of the acquired disease. Numbers of instances have been recorded in which the nurse has been infected with syphilis, a chancre forming on the breast, the virus being communicated from the lesions in the child's mouth. It is impossible to lay too much stress upon this point. The discharges from the mucous patches, and probably from all the lesions on the skin and mucous surfaces, contain the syphilitic poison. A syphilitic child should never be suckled by any other person than its own mother. If she is unable to feed it, it should be brought up by hand, and the most scrupulous care should be taken that other children do not use the bottle or spoon with which it is fed. For the same reason, healthy people should not be allowed to kiss or fondle a syphilitic child, although in the more marked and severe cases this caution is perhaps unnecessary, for syphilitic children are eminently repugnant and loathsome. In order to emphasise the terrible consequences which may result from allowing a syphilitic infant to be suckled by a healthy nurse, I may quote the following from Diday:—

'A foundling in Brussels was placed with a woman named Hauwaert, at Alsemberg. After some time she had an affection of the breasts, and as they were distended she had them drawn by her son, who was ten years of age. He succeeded so well in this that several other women, having occasion to take advantage of his talent, applied to him for the same service. Several of them became infected in this manner, amongst others a woman named Demol, who contracted ulcers on the breasts. Being herself nursing, she communicated to her child, which was being suckled by her, excoriations on the lips and in the mouth. Being ignorant of the nature of these ulcers, she accidentally gave the breast to the child of her sister, named Deraw. A short time afterwards this latter child had chancres in the throat and venereal pustules on the body; the mother also had chancres in the throat and on the breasts, and moist pustules in the vulva and about the anus. Her eldest daughter, having put into her mouth the spoon with which she had been giving some broth to her young brother, also became infected, and contracted ulcers in the throat. The husband, having cohabited with his wife, became affected with flat pustules and a chancre in the throat.

Seutin, passing through this commune, and informed of the disease which was preying upon several of its inhabitants, submitted all the persons infected to a strict and minute examination. He concluded from it that the author could be no other than the boy Hauwaert, the victim, as well as his mother, of the foster-child brought from Brussels. And, in fact, when this boy came to be examined, he was found to be the subject of a vast indurated chancre in the throat, and of a perforation of the palate, the consequence of an eroding ulcer.' [1]

And here I should point out that the mother of a syphilitic child, although she may not have manifested any symptoms of the disease, never, so far as is known, contracts the disease from her own child. This remarkable fact was pointed out by the late Dr. Colles of Dublin and is known as Colles's law, His statement is as follows:—'One fact well deserving our attention is this: that a child born of a mother who is without obvious venereal symptoms, and which, without being exposed to any infection subsequent to its birth, shows this disease when a few weeks old—this child will infect the most healthy nurse, whether she suckle it, or merely handle and dress it; and yet this child is never known to infect its own mother, even though she suckle it while it has venereal ulcers of the lips and tongue.' [1] So far as I know, no absolutely conclusive and well-authenticated exception to Colles's law has as yet been published. In those cases in which the mother has presented no symptoms or signs of syphilis, it seems certain that she has been protected by the syphilitic infant *in utero*. It is usually supposed that this protection is due to the absorption from the fœtus (the placental blood) of an attenuated virus or the products of an attenuated virus.

In addition to these general measures, the child should be well clothed and protected from cold and all depressing conditions. Anything likely to produce irritation of the bowels should be carefully avoided; during the stage of marasmus, vomiting and diarrhœa are often prominent symptoms. In older children, cod-liver oil and the syrup of the iodide of iron are often valuable remedies. After a prolonged course of antisyphilitic remedies, arsenic and iron are often useful, especially in those cases in which the patient is cachectic and anæmic.

Etiological Considerations. — Before concluding this article, let me say a word or two with regard to the etiology of the disease.

We have seen that in congenital syphilis there is no primary sore, that during infancy the symptoms for the most part belong to the secondary period, and that subsequently (during later childhood, youth, or early adult life) tertiary symptoms may be developed.

Syphilis may be communicated to the child at the period of conception. It is unnecessary to say that in the great majority of cases in which the child inherits congenital syphilis, the father has contracted the disease before marriage.

When either of the parents is affected with primary or secondary syphilis at the time of conception, the child will probably, but not necessarily, inherit the disease.

When both parents are actively suffering from syphilis, the child is more likely to inherit the disease than when one parent only is affected.

When one or both parents are actively suffering from the disease (the subject of manifest primary or secondary symptoms) at the time of conception, there is a much greater chance of the child inheriting the disease than in other cases in which one or both parents have previously had syphilis but in which there are no active symptoms in either parent at the time of conception.

The closer conception follows the primary and secondary stages of the disease in the parents, the greater is the risk to the child.

With the lapse of time, the risk of the disease being transmitted to the children gradually diminishes. Speaking generally, the first children which are born after syphilis is acquired by one or both parents are more severely affected than the succeeding children. There may be first one or more miscarriages, then one or more dead-born children, then one or more children who die soon after birth, then one or more children born at the full time who manifest the characteristic symptoms of infantile syphilis, and then a series of healthy children. Exceptions to this rule are not by any means uncommon. Antisyphilitic treatment of the parents prior to conception and of the mother during one pregnancy may protect the product of that pregnancy, but if the treatment is

[1] *Infantile Syphilis*, New Sydenham Society's Translation, page 167.

[1] *The Works of Abraham Colles*, edited by Robert M'Donnell, the New Sydenham Society, London, 1881, chap. xiii. p. 287.

suspended, the product of the next pregnancy may be syphilitic.

When the disease in the parents is actively treated, the risk of transmission to the children is less than when it is untreated.

When the mother is actively syphilitic at the time of conception (the father being unaffected), there is a greater risk of the child inheriting the disease than when the father is actively syphilitic at the time of conception and the mother unaffected. This is probably due, in part at least, to the fact that in cases of this kind the child runs a double risk of infection, viz., at the time of conception through the germ-cell and during the whole course of pregnancy through the maternal blood.

If the mother contracts syphilis during pregnancy, at all events up till the sixth or seventh month, the child usually becomes affected. It is doubtful if the child is ever affected when the mother contracts syphilis after the seventh month, the father of course being unaffected.

It is certain that a man who has recently suffered from syphilis, but who at the time of marriage presents no active lesions, may transmit the disease to the child, and the child while *in utero* may transmit the disease to the mother. In some of the cases which at first sight appear to be cases of this kind, the mother has no doubt been directly infected by the husband and the symptoms of the disease have not been noticed prior to pregnancy. But this is not always so. It is certain that in many cases the mother does not manifest any syphilitic symptoms until she becomes pregnant. In many of these cases, as Fournier has so clearly pointed out, the pregnancy is the only factor which accounts for the syphilis in the mother. She has evidently been infected by the child *in utero* which has derived its syphilis from the father (syphilis *by conception*).

Further, in some cases, but they are probably rare, the mother of a syphilitic child does not manifest any symptoms of syphilis either prior to, during or after pregnancy. Nevertheless, as I have already remarked, she is protected against the disease; she cannot contract a primary sore from her syphilitic child as a healthy nurse can do.

It would, therefore, appear (1) that the child may become infected through the placental circulations, i.e. through the maternal blood, as in those cases in which the mother contracts the disease during pregnancy and in which the father was healthy at the time of conception; and (2) that the mother may become infected through the placental circulation, i.e. through the blood of the fœtus which is syphilitic by inheritance (infected by the sperm-cell of the father at the time of conception); and (3) that the mother may be protected (inoculated with a virus of diminished intensity) by the syphilitic fœtus *in utero*.

Whether the child may be infected and protected in the same latent way while *in utero*, i.e. by the gradual absorption from the blood of the mother of an attenuated syphilitic virus, is not known, but theoretically there seems every reason to suppose that this may occur.

Children who have inherited congenital syphilis may undoubtedly contract primary syphilis in adult life; but it is probable that, theoretically speaking, they are less liable to contract the disease than healthy, non-syphilitic persons; and that, if they do contract the disease, it will probably in them be less severe than in the average run of healthy persons. It is doubtful if the disease is ever handed on to the third generation (i.e. whether the children of patients affected with congenital syphilis are ever syphilitic in consequence of the congenital syphilis of their parent or parents). The question is obviously one which is very difficult to prove. There are many clearly sources of fallacy (such as one or other of the parents having contracted the acquired form of the disease). Mr. Hutchinson has reported one case in which there seemed some reason to suppose that the disease was handed down to the third generation; but he adds that this single fact must be received with great scepticism. If further observation shows that such a form of transmission does actually occur, it will indeed be very remarkable. I know of nothing analogous to it in the whole range of pathology—the virus of an infective disease retaining its vitality in the human body through two generations.

The considerations which have been advanced above undoubtedly show that syphilis may be transmitted either through the sperm-cell, the germ-cell, or through the blood of the mother (as in those cases in which the mother contracts syphilis at the time of conception and in which the child subsequently manifests the disease). It has also been suggested that the child may contract syphilis from the vaginal passages at the time of its birth; but, so far as I know, no well-authenticated case of this kind has been put on record. The vernix caseosa seems to protect the skin of the child from the absorption of the syphilitic virus. Mr. Hutchinson supposes that when syphilis is transmitted at the moment of conception through the sperm-cell, the transmission must consist in the passage of a particulate virus. In opposition to this supposition it has been argued that the semen when inoculated into the tissues of a healthy subject is incapable of propagating the disease. But into this and many other debatable but interesting theoretical questions connected with congenital syphilis I need not enter.

DESCRIPTION OF PLATE LXXX.—A typical case of congenital syphilis.

The patient, a boy aged 16, was seen at the Edinburgh Royal Infirmary on 14th February, 1889. He was 'delicate' as an infant and suffered from 'snuffles.' He was small for his age and knock-kneed. His nose was sunken and the nostrils filled with crusts; he had suffered from ozena for eight years. The left cornea was opaque, the result of keratitis. The central incisors in the upper jaw were characteristically misshaped. There were scars, the results of old ulcerations, at the angles of the mouth. The frontal eminences were prominent. The skin had not the pale earthy tint characteristic of congenital syphilis; indeed, the face was well coloured. (The artist has rather exaggerated this in the drawing.)

Under mercury and iodide of potassium, marked improvement rapidly took place.

DESCRIPTION OF PLATE LXXXI.—Congenital syphilis.

This plate represents a remarkable case of congenital syphilis. The details of the case are as follows:—

F. A., aged 42 years, an inmate of the Craiglockhart Poorhouse, was seen on several occasions with Dr. Edward Carmichael to whom I am also indebted for allowing my artist—Mr. John Williamson—to paint the case.

Past History.—His father and mother were both drunkards; his history during early infancy is unknown.

He was first admitted to the Edinburgh City Poorhouse when four years of age. At that time, the nasal bones were evidently diseased; for the woman who nursed him, and who is still an inmate of the Poorhouse, says that a small hole was present in the side of the nose in the position of the large opening shown in the plate; she states that the discharge from this sinus was very offensive and that the doctor (Dr. Smith) used to wash it out daily with a small brush.

Between the ages of 9 and 15, he was boarded out at West Linton. At the age of 15, he was re-admitted to the Poorhouse because of sores on the forehead and head. He has been an inmate of the Poorhouse or of Morningside Asylum (he has twice been sent from the Poorhouse to the Asylum) ever since. He has never been able to do anything for himself.

When asked whether he has ever had any venereal disease, he stoutly maintains that he has not. He says that many doctors have asked him the same question. He says that his imperfect health is the result of the mercury which was given to him in large quantities during childhood.

Present condition.—The patient looks much older than his years. His appearance is very peculiar. He is very short and small; his height is 4 feet 6 inches, and his weight 4 st. 7 lbs. The bones are very small and thin, and the muscles very poorly developed. He walks with a duck-like, waddling gait; the spine is curved forwards in the dorsal and lumbar regions, the shoulders being thrown far back so that a line dropped from the seventh cervical vertebra falls almost beyond the sacrum. The appearance which the patient presented in the erect position is shown in Plate LXXXII., fig. 3.

The head is well shaped; it looks proportionately somewhat large for the body. The forehead is studded with irregular, white, ivory-like projections (see Dr. Alexis Thomson's report on the skull which is given below).

The skin has a sallow, earthy hue.

The eyes are large and slightly protruding. The corneæ are clear. A cataract is present in the left eye, which is turned outwards (divergent strabismus). The ears, which are large, stand out from the head.

The nose is pug-shaped and sunken at the bridge; a large oval perforation is present at the root of the nose on the left side.

The palate is highly arched and there is a small perforation in it. Almost all the teeth, including the central incisors in the upper jaw, are wanting.

The hair is scanty and flax-like.

The elbow joints are thickened and the ulnæ show evidences of old syphilitic disease.

His memory is defective and his intellectual powers very imperfectly developed. He is subject to delusions, one of which is that he is a doctor of divinity.

The speech is defective and the tone suggestive of a cleft palate.

The genital organs are very imperfectly developed.

MEASUREMENTS.

Circumference of head, ...	20 inches.
Antero-posterior measurement of the head (from the root of the nose to the occipital protuberance), .	11 „
From the chin to the root of the nose, ...	7 „
Girth of chest, ...	27 „
From the seventh cervical vertebra to the top of the coccyx, ...	11 „

Dr. Alexis Thomson's report on the post-mortem condition of the skull and ulnæ.

The patient died from an attack of facial erysipelas in the year 1892. Through the kindness of Dr. Carmichael I was enabled to make a post-mortem examination. Dr. Alexis Thomson kindly examined the skull and ulnæ and favoured me with the following report on their condition:—

'The skull and ulnæ, which you were good enough to send for my inspection, would appear to have belonged to a small, aged subject, probably a female' (I purposely abstained from giving Dr. Thomson any account of the life history lest I might prejudice his opinion regarding the bone condition), 'who had suffered in earlier years from tertiary syphilis and who within a comparatively recent period before death had sustained a fracture of both forearms.

'The skull is below the average size and is well formed. The sagittal and coronal sutures are in process of obliteration. There are marked evidences of former bone-disease in certain areas of the cranial vault and in the nose and palate.

'The outer surface of the calvaria is more porous than normal from increased vascularity of the pericranium. In the outer table of the vertical plate of the os frontis, over a circular area extending in the sagittal plane from immediately above the level of the supra-orbital ridges to the coronal suture, and in the coronal plane to within 1·5 cm. of the temporal ridge on either side, the surface is very uneven, largely occupied by scattered flattened elevations, of which some are sharply outlined, circular, or made of circles, smooth and button-like; while amongst these there are other, less prominent, elevations of irregular outline, presenting a grooved and fissured surface. Between and around these elevations, there are a number of comparatively large circular or oval depressions with shelving walls and smooth floor. Close to the bregma there is a solitary, flat-topped, button-like elevation of which the edge overhangs the surrounding bone.

'The outer table of the parietal bones, in the region comprised between their eminences and the lambdoidal suture, presents similar, though less pronounced, alterations. On the right side between the parietal eminence and the sagittal suture, there is an oval depression, measuring 4 cm. by 3 cm., the long axis being in the coronal plane with shelving uneven floor and in its centre a minute linear perforation. In the corresponding region of the left parietal, there are several shallow depressions and tuberculated elevations.

'The maximum thickness of the bone as measured in the same section is 6 mm. No spongy bone or diploë intervenes between the two tables. The inner table, beyond the perforation referred to in the right parietal bone, shows throughout an exaggeration of the normal vascular grooving, more especially in the immediate vicinity of the sutures. The grooves for the meningeal arteries are shallower and less defined than in an average skull. There are several pacchionian depressions on either side of the groove for the superior longitudinal sinus.

'The foramina for the emissary veins are well marked.

'In the face, the nasal bones, the nasal processes and the posterior half of the palatine processes of the superior maxillæ, the greater part of the vertical plate and of the middle turbinates of the ethmoid, the inferior turbinates, the vomer, and the horizontal plate of the palate bones have for the most part disappeared so that the nasal bridge and septum, and the canal for the lachrymal sac and nasal duct on the left side, no longer exist, and there is a large gap in the hard palate. The lower jaw presents the usual changes associated with loss of the teeth.

'The ulnæ show evidences of antecedent syphilis, senile atrophy and recent fracture. The left ulna has been fractured through the middle of its shaft; union is incomplete without any external or ensheathing callus; the fragments meet each other at an angle of 140°, forming an angular projection posteriorly. In the right ulna the fracture which is situated at the junction of the upper and middle thirds of the shaft, is more completely united, with a considerable amount of ensheathing callus and scarcely any angular deformity. The outlines and surfaces of the bones as a whole are uneven and irregularly tuberculated from antecedent periostitis, while the articular margins and surfaces are similarly altered from previous disease involving the elbow joints.

'Both ulnæ are very slender (atrophied or under-developed).'

DESCRIPTION OF PLATE LXXXII.—Congenital syphilis.

Fig. 1. This photograph represents the boy and his mother whose cases are recorded on page 491. The boy's tongue could not be fully protruded; it is wrinkled and atrophied; its tip is turned to the left side. A round, tertiary, syphilitic ulcer is present on the left forearm of the mother.

Fig. 2. This figure, which is copied from Ricord, shows the body and limbs of an infant covered with a syphilitic eruption at the time of birth.

Fig. 3. This drawing represents the case of congenital syphilis which is figured in Plate LXXXI.

Fig. 4. Syphilitic teeth.—(After Jonathan Hutchinson.)

Fig. 5. This photograph represents a typical case of congenital syphilis. The patient, a man aged 27, was seen at the Edinburgh Royal Infirmary on November 10th, 1886. He was suffering from scabies. He stated that his general health was perfectly good, but his eyesight was very defective; both corneæ were opaque from former keratitis. The nose was markedly depressed at the bridge. The single central incisor which was present in the upper jaw was typically misshaped. The forehead was broad and the frontal eminences prominent. Several linear cicatrices were present at the angles of the mouth. The lower lip was cracked and ulcerated in the centre.

The patient could give no account of his health during infancy and childhood; but he stated that his nose became misshaped either soon after birth or during early childhood. At the age of 11, he suffered from an affection of the eyes (syphilitic keratitis) and was almost blind for two years. After this his sight improved. The left cornea had cleared considerably, the right was still very opaque.

The patient had one sister younger than himself; she died when three years of age; he does not know the cause of death. He does not know whether his mother had any miscarriages. He has six half-brothers and sisters, all of whom are strong and healthy. His father married a second time, a few years after the death of his mother. His father died, he says, at the age of 49 from blood-poisoning, and his mother at the age of 30 from inflammation of the bowels.

Fig. 6. The patient whose legs are represented in this figure was a girl aged 15. She was seen at the Edinburgh Royal Infirmary in September, 1890. She was suffering from periostitis of both tibiæ and amyloid disease of the liver, spleen and intestines.

No definite history could be obtained of the state of the patient's health during infancy, but she stated that her voice had always been hoarse.

When five years old, she began to suffer from pain in the knees and swelling of both knees (syphilitic synovitis) Two years later, the elbow joints swelled and became painful. For the past five years, the legs have been affected Both tibiæ are markedly thickened, elongated and curved; they are very painful and tender to the touch None of the affected bones have suppurated

The physiognomy is not characteristic of congenital syphilis, though the complexion is earthy-coloured The teeth are very irregular, but the central incisors in the upper jaw are not notched. The corneæ are quite clear. The liver is greatly enlarged, smooth and hard; its lower border reaches the umbilicus; the upper level of the liver dulness corresponds to the 4th rib. The spleen is also considerably enlarged. For the past three months, the patient has suffered from constant watery diarrhœa. There are sometimes as many as ten motions in the course of the twenty-four hours.

The patient is extremely emaciated. Her height is 4 ft. 5½ in., and her weight 3 st.

The temperature is subnormal; the lungs are quite healthy; there are no indications of tubercle.

Under large doses of iodide of potassium, the periostitic pains were relieved. The patient was then lost sight of. The future progress of the case is not known.

DESCRIPTION OF PLATE LXXXIII.—Congenital syphilis.

Figs. 1 and 2. These photographs represent the case of congenital syphilis described on page 59. The patient's facial appearance is in no way characteristic of congenital syphilis. He was a well-grown, well-developed, healthy-looking lad. The central incisors in the upper jaw are normally shaped. A large perforation is present in the soft palate.

Fig. 3. This photograph represents the sister of the patient represented in fig. 1. Her facial appearance is characteristic of congenital syphilis. The nose is sunken; the forehead broad; the corneæ were opaque; the central incisors in the upper jaw typically syphilitic; the patient was very deaf; she suffered from epilepsy and dementia.

Figs. 4 and 5. These figures represent a typical case of congenital syphilis with extensive disease of the palate.

The patient, a boy aged 15, was seen at the Edinburgh Royal Infirmary on 1st February, 1889. He complained of difficulty in swallowing and sore throat. His throat had troubled him for several years. The uvula had been ulcerated away. The soft palate was adherent to the posterior wall of the pharynx. A narrow slit-like opening passed from the cavity of the mouth to the pharynx. The mucous membrane of the pharynx was thickened, in places ulcerated and covered with fungating granulations. The tonsils seemed to have disappeared.

The nose was sunken. There were scars at the angles of the mouth. The central incisors in the upper jaw were not misshaped. The corneæ were clear. Under the lobe of the left ear and on each side of the neck there were raised keloid patches which represented the cicatrices of former ulcerations.

Fig. 6. This photograph represents a typical case of congenital syphilis in which extensive ulceration of the neck, face and ear had occurred. A long tag of skin remains attached to the ear.

The patient, aged 21, was seen at the Edinburgh Royal Infirmary on 14th June, 1889. He was short and stunted in size. His nose was sunken. The soft palate was ulcerated and destroyed. There was a depression in the frontal bone. The lateral incisors in the upper jaw were very markedly peg-shaped; the single incisor which was present was narrow and screw-driver shaped but not notched. The corneæ were clear. The patient was very delicate as an infant and had been delicate all his life.

PROGRESSIVE MUSCULAR ATROPHY

Synonyms.—Wasting palsy; Poliomyelitis anterior chronica; The aran-duchenne type of progressive muscular atrophy; and The spinal or myelopathic form of progressive muscular atrophy.

THE patient represented in Plate LXXXIV. was under my observation for several years. The case is a typical example of the spinal or myelopathic form of progressive muscular atrophy. The essential features of that disease are:—(1) gradual and progressive muscular atrophy; (2) loss of muscular power, which roughly speaking is proportionate to, and which is developed contemporaneously with the atrophy; and (3) the absence of sensory disturbances and of any affection of the bladder or rectum. In the great majority of cases, the atrophy commences in the small muscles of the hand and subsequently extends to other muscles. The atrophy is attended with the presence of fibrillary tremors and, at a certain stage of its development, by the imperfectly developed form of the reaction of degeneration. The disease is essentially chronic. It usually commences during the middle period of adult life and is much more common in men than in women. Before describing its clinical features in detail, it may be well to consider its pathological anatomy and etiology.

Pathological Anatomy.—The essential pathological substratum of the ordinary form of progressive muscular atrophy is a slow and gradual destruction of the multipolar nerve cells in the anterior horn of the spinal cord. In some cases, the lesion is *limited* to the region of the anterior horn, at least so far as the clinical symptoms enable us to judge. It is for this reason that the disease is included under the system lesions or diseases of the spinal cord. In other cases, in which the symptoms are characteristic of progressive muscular atrophy, the crossed pyramidal tracts (sometimes also the direct pyramidal tracts), are also implicated. The indications of this sclerosis are not always very apparent during life; but it is said that in many of the cases in which there are no symptoms indicative of a lesion of the crossed pyramidal tracts during life, the pyramidal tracts are distinctly sclerosed after death. Indeed some authorities suppose that the sclerosis of the crossed pyramidal tracts is not merely an associated lesion or complication, but that it is an essential and constant feature of the disease. The question is still *sub judice*, but cases are undoubtedly met with in which there is absolutely no sclerosis in the crossed pyramidal tracts after death.

If then we look at the matter from the standpoint of the clinician, it must, I think, be admitted, *firstly*, that in some cases of progressive muscular atrophy there is no definite clinical evidence (in the form of spastic symptoms and exaggeration of the deep reflexes either in the upper or lower extremities) of any sclerosis in the crossed pyramidal tracts during life; and *secondly*, that in other cases in which the characteristic symptoms of progressive muscular atrophy are well marked, very definite indications of a lesion in the crossed pyramidal tracts (marked exaggeration of the knee-jerks, ankle clonus and perhaps rigidity and tension of the muscles either in the upper or the lower extremities) are present.

The illustrious Charcot attached great importance to these clinical differences. He applied the term *amyotrophic lateral sclerosis* to some of the cases of progressive muscular atrophy in which there is a well marked lesion of the crossed pyramidal tracts. He supposed that in amyotrophic lateral sclerosis the lesion commences in the crossed pyramidal tracts and, after a time, extends to the anterior horn. According to Charcot, the lesion of the anterior horn in amyotrophic lateral sclerosis is secondary, or, as he termed it, *deuteropathic*; whereas in progressive muscular atrophy, the lesion of the anterior horn is primary or *protopathic*.

But as I have already pointed out, the correctness of this view has of late years been called in question. Leyden and Gowers believe that there is no real distinction (no absolute pathological line of demarcation) between progressive muscular atrophy and amyotrophic lateral sclerosis; they are merely varieties of the same disease; the typical forms which seem to be distinct run insensibly one into the other and are connected by intermediate and less typically differentiated varieties.

But whether we accept this view or not—and personally I do not see my way to accept it—it is, I think, advisable for clinical purposes to differentiate the two varieties and to divide cases of progressive muscular atrophy into two great groups, viz., (1) Cases in which the lesion in the anterior horn is the only or the predominant lesion and the muscular atrophy is the only or the predominant symptom; and (2) Cases in which definite clinical indications of a lesion in the crossed pyramidal tract (muscular rigidity and tension or marked exaggeration of the deep reflexes) are also present. The first group comprises the ordinary (spinal) form of progressive muscular atrophy; the second group the condition which Charcot termed amyotrophic lateral sclerosis.

The character of the lesion.—The points which I wish chiefly to emphasise are:—that the spinal form of progressive muscular atrophy is essentially due to a slow and gradual destruction of the multipolar nerve cells in the anterior cornua of the spinal cord; that in many cases the crossed pyramidal tracts are also sclerosed; that in some cases the sclerosis of the crossed pyramidal tracts is so marked that the symptoms which it produces form a conspicuous feature of the clinical picture.

The question has been much debated whether the lesion of the nerve cells is degenerative or inflammatory in character.

In some cases, subacute or chronic inflammatory changes in the grey matter of the anterior horn are undoubtedly present. The presence of such inflammatory changes in the anterior horn does not necessarily prove that the primary lesion of the nerve cells is inflammatory; for inflammatory changes are frequently developed in tissues which are degenerated and diseased. In the present state of our knowledge it is perhaps impossible to pronounce a definite and dogmatic opinion and to say whether the Aran-Duchenne form of progressive muscular atrophy is the result, on the one hand, of a degenerative atrophy of the multipolar nerve cells with secondary inflammatory changes in the neuroglia, or, on the other, of a chronic parenchymatous inflammation of the anterior horn of grey matter, the essential feature of which is a destruction and degeneration of the multipolar (motor) nerve cells.

The mode of extension of the lesion.—In the next place it must be noted that the lesion is not diffused all through the spinal cord; it is limited to certain definite regions and segments. This is a most important clinical characteristic of the spinal (Aran-Duchenne) type of progressive muscular atrophy.

In the great majority of cases, the lesion commences in the lower cervical or first dorsal segments. The nerve cells connected with the small muscles of one or both hands are usually first involved. In this respect, progressive muscular atrophy contrasts remarkably with poliomyelitis anterior acuta. In that disease, the lumbar is much more frequently affected than the cervical enlargement and the paralysis consequently affects the muscles of the legs much more frequently than those of the arms.

In many cases the atrophy commences in the thenar or hypothenar muscles of the right hand. The movements of the fingers and thumb are more highly specialised than any other of the limb movements; and mechanisms which are very complicated in structure and highly specialised in function are easily deranged. It would appear, too, that degenerative processes are more apt to develop in the neuro-motor mechanisms which are complex and highly specialised than in the neuro-motor mechanisms which are simple in structure and more automatic in function.

In exceptional cases the atrophy seems to commence in the muscles of the back or lower extremities. But this mode of development perhaps requires further verification. It is only of recent years that a definite distinction has been drawn between the spinal or myelopathic and the idiopathic or myopathic forms of progressive muscular atrophy; and it seems certain that in the great majority of cases of the Aran-Duchenne type, the small muscles of the hand are first affected. I shall return to this point in connection with the clinical history.

In the great majority of cases, the lesion at its commencement seems chiefly to involve the nerve cells in one, usually the right, anterior horn; consequently the atrophy is, at its commencement, usually more marked, or only marked in the small muscles of one, usually the right, hand.

In the course of a short time, the lesion extends to other half segment or segments.

It usually (next) involves the nerve cells in the opposite half of the segment which was first affected, i.e. when the small muscles of one (say the right) hand are first involved, the small muscles of the opposite (the left) hand are next affected. But this is not always the case. In some cases, other half segments on the same side of the cord (cervical region) are next affected; in other words, in some cases the small muscles of one (say the right) hand are first involved, and the muscles of the forearm or deltoid on the same (the right) side—not the muscles of the opposite (the left) hand, as is usually the case—are next implicated.

The next point in the pathology which should be noted is that all of the nerve cells in the particular half of the segment which is first affected are not simultaneously involved. The lesion picks out, as it were, some nerve cells, and after slowly and gradually destroying them, passes on to, picks out and destroys other nerve cells. The destructive process is slow. The individual nerve cells which are first affected are slowly destroyed. Months, it may be years, elapse before all the nerve cells in the area of the cord which is first involved are all destroyed; in fact, the destruction is rarely, if ever, complete; some of the nerve cells almost always remain.

The results of this slow and gradual destruction is the production of muscular weakness, atrophy, and ultimately of paralysis of the muscles connected with the affected segments of the cord. The weakness and muscular atrophy are, it will be observed, slowly and gradually developed. In this respect progressive muscular atrophy contrasts remarkably with poliomyelitis anterior acuta. In that disease the paralysis is rapidly developed, the maximum extent of the paralysis is at once produced, and, in the great majority of cases, some of the initial paralysis disappears after the acute inflammatory changes have subsided. It is the exact reverse in progressive muscular atrophy. In that disease, the lesion commences in a very insidious manner, slowly and gradually destroys a few nerve cells, produces little or no obvious derangement at first, but gradually extends and finally involves almost all of the nerve cells in the affected segment, and it may be ultimately produces complete atrophy and loss of power.

Further, in poliomyelitis anterior acuta the lumbar is more frequently affected than the cervical enlargement; whereas in progressive muscular atrophy the cervical enlargement is almost invariably affected, and the lumbar enlargement usually escapes. Again, poliomyelitis anterior acuta is essentially a disease of the child, whereas progressive muscular atrophy is essentially a disease of the adult. A further point of distinction is this, that in poliomyelitis anterior acuta the lesion remains limited to the segments of the spinal cord which were first attacked; but in progressive muscular atrophy the lesion tends to spread to other segments until it may ultimately involve almost every segment in the cervical enlargement. Indeed, it not unfrequently happens that the dorsal and sometimes the lumbar segments are ultimately invaded; in many cases the multipolar (motor) nerve cells in the medulla oblongata are finally implicated.

From these statements it will be seen that the two diseases present a remarkable contrast in respect to the pathological character of the lesion and the clinical features and course.

Naked-eye appearances of the spinal cord.—On examining the cord from a case of progressive muscular atrophy, the most obvious alteration is the grey and wasted condition of the anterior nerve roots. In one typical case in which I obtained a post mortem a few years ago, the contrast between the atrophied anterior and the normal posterior nerve roots was most striking, not only in the cervical, but in lumbar region of the cord. In that case the lower extremities were markedly affected. Transverse sections of the cauda equina, after hardening, showed this contrast in a very remarkable way.

With the exception of the grey and atrophied condition of

the anterior nerve roots there is little or nothing to be seen with the naked eye. In some cases the grey matter of the anterior horn is said to be softer than normal.

Microscopical appearances of the spinal cord.—On examining properly hardened sections the essential change is seen to be an atrophy, and in the advanced stages of the disease it may be the disappearance, of almost all of the multipolar nerve cells in the anterior horn of the segment or segments of the cord which are chiefly implicated (see Plate LXXXV., figs. 1 and 2). The atrophy seems in some cases to be a simple atrophy; the nerve cells are shrivelled, smaller and less plump than normal; they stain badly; their processes are fewer in number than normal, and in the advanced stages of the disease the processes have entirely disappeared. In some cases, it is said that the nuclei still remain in the centre of the atrophied cells. In many cases an excess of pigment is deposited in the shrivelled cells. In short, the essential change in the nerve cells is atrophy, pigmentation, and degeneration.

The minute nerve fibres and the axis-cylinder processes of course share in this degeneration.

The connective tissue (neuroglia) in which the nerve cells are embedded is usually increased in amount (sclerosed), and the connective tissue cells (the Deiters' cells) enlarged. The blood vessels in the affected area are often dilated, their walls thickened, and their hyaline sheaths larger and more capacious than normal.

In cases which run an unusually rapid course, fatty granules may be present in the nerve cells or in the spaces which were formerly occupied by nerve cells. But it is doubtful if this fatty change occurs in the ordinary typical (chronic) cases.

In those parts of the cord in which the lesion is less advanced, many healthy nerve cells may still be seen.

The anterior nerve roots connected with the less severely affected parts of the cord do not present the extreme grey atrophy which the nerve roots connected with the lower part of the cervical enlargements usually exhibit.

The degeneration extends through the nerve roots and peripheral motor nerves down to the muscles.

As I have already stated, the crossed pyramidal tracts (and, I may add, the anterior pyramidal tracts), are in many cases sclerosed. Indeed, there may be some increase of the connective tissue through the whole transverse thickness of the cord. Nevertheless, the posterior horn of grey matter, the posterior roots and posterior columns are, practically speaking, always healthy.

In many cases the sclerosis of the crossed pyramidal tracts is only slight; in some cases it is entirely absent.

In cases of amyotrophic lateral sclerosis, the sclerosis of the pyramidal tracts extends throughout the whole length of the cord, and, indeed, higher up, into the medulla, pons Varolii and it may be even through the crus cerebri and internal capsule to the cortex itself.

In those cases in which there is a lesion both in the anterior cornua and the crossed pyramidal tracts the sclerotic lesion in the crossed pyramidal tracts is clearly not the cause of the lesion in the anterior horn; for, as I have already pointed out, cases are frequently met with in which, so far as the clinical evidence shows, the lesion seems to be entirely limited to the anterior horn and in which there are no symptoms indicative of a lesion in the lateral columns. Further, we know that in primary spastic paraplegia and in cases in which the crossed pyramidal tracts are affected with secondary descending degeneration, the lesion in the crossed pyramidal tracts is not, unless in quite exceptional instances, attended with any degeneration of the multipolar nerve cells in the anterior horn of grey matter.

According to another view the lesion in the crossed pyramidal tract is secondary to the lesion in the anterior horn. The fact that in poliomyelitis anterior acuta, acute destruction of the nerve cells of the anterior horn and acute inflammation of the anterior horn is not followed by sclerosis in the crossed pyramidal tracts, seems strongly opposed to this theory.

A third view supposes that the two lesions are not directly related as cause and effect, but that they are simultaneously developed, and are probably due to a common cause acting upon the whole motor tract. If this is so, we would not expect to find any direct relationship, as regards severity, between the muscular atrophy (the clinical manifestation of the lesion in the anterior horn) and the rigidity and tension (the clinical manifestations of the lesion in the pyramidal tracts); and such is the case.

I have already stated that in some cases of progressive muscular atrophy, the lesion extends to, and involves, the motor nerve cells of the medulla oblongata, and it may be of the pons Varolii. This is one of the most important points connected with the morbid anatomy and the clinical history of the disease; for involvement of the cardiac and respiratory centres in the medulla oblongata is a frequent cause of death. In some cases in which progressive muscular atrophy in the limbs and trunk and bulbar symptoms are combined, the spinal nuclei are first involved; in others, the bulbar nuclei are first affected; while in a third group of cases the spinal and bulbar nuclei are simultaneously affected. I repeat, that so far as we know, the lesion in the medulla oblongata, which is the pathological substratum of glosso-labio-laryngeal paralysis is identical with the lesion in the cord which is the pathological substratum of progressive muscular atrophy. In both cases the lesion is a degeneration of the motor (multipolar) nerve cells. In both affections the pyramidal tracts are frequently involved.

It was at one time supposed that progressive muscular atrophy was due to a lesion of the sympathetic; but we now know that this view was a mistaken one.

Further, the theory which was strenuously supported by Friedreich, viz., that the primary cause of the disease is situated in the muscles, has been proved to be erroneous. As I have already sufficiently pointed out, pathological investigation has conclusively proved that the Aran-Duchenne type of progressive muscular atrophy is due to a lesion of the multipolar nerve cells of the anterior cornua of the spinal cord.

The naked-eye and microscopical appearance of the muscles.—In advanced cases the muscles are pale and fawn-coloured; they may look as if they were almost entirely composed of fat. The muscular wasting seems to be essentially a simple atrophy. So far as is known, enlargement of the muscular fibres which is such a conspicuous and characteristic feature of many cases of the myopathic (idiopathic) forms of muscular atrophy does not occur.

In advanced stages of the disease, microscopical examination shows that the muscular fibres have almost entirely disappeared. In the earlier stages, some of the muscular fibres are found to be healthy; others present various stages of atrophy. The essential change seems to be a simple atrophy muscular fibres which are markedly atrophied and narrowed

may still retain their transverse striation. In the advanced stages, the transverse striation may completely disappear, and the muscular fibres may be infiltrated with granular and fatty globules. The muscle nuclei may be increased in number. Some authorities state that some of the muscular fibres are sometimes affected with a colloid or hyaline degeneration. The spaces between the individual muscular fibres may be occupied by an excess of connective tissue, dilated blood vessels and a few fat cells; but the increase of the connective tissue is not, as a rule, so marked as it is in many cases of poliomyelitis anterior acuta, and is always far less apparent than in pseudo-hypertrophic paralysis.

Etiology.—Progressive muscular atrophy usually commences between the ages of thirty and fifty. The disease is very rare before the age of twenty-five, and exceedingly rare in childhood. I refer to the typical spinal (Aran-Duchenne) form of the disease. The idiopathic (myopathic) forms of muscular atrophy which in the great majority of instances commence in childhood or youth, must, as I have already pointed out, be carefully distinguished from the common spinal form of progressive muscular atrophy which we are now considering.

Progressive muscular atrophy comparatively seldom commences after the age of fifty. In this respect it presents a remarkable difference from glosso-labio-laryngeal paralysis, for that disease rarely develops before the age of fifty.

Progressive muscular atrophy is much more common in men than in women. It seems to attack the lower orders of society more frequently than the upper. At one time it was supposed that the disease is often directly inherited, but we now know that this view is a mistaken one. The Aran-Duchenne type of progressive muscular atrophy is very rarely, some authorities say never, directly inherited. In this respect the spinal or myelopathic form of progressive muscular atrophy differs very markedly from the idiopathic or myopathic forms of muscular atrophy (pseudo-hypertrophic paralysis, the juvenile form of Erb and the allied facio-humeral type of Landouzy and Dejerine) in all of which, and in the peroneal type of progressive muscular atrophy which is probably neuropathic or myelopathic, the disease can often be traced through several succeeding generations.

We know little as to the exact cause of the degenerative or inflammatory lesion which is the pathological substratum of the ordinary (spinal) form of progressive muscular atrophy. Many conditions have been blamed in individual cases, but great caution is necessary in drawing conclusions on this point. The onset is so insidious that in many cases the disease has already been in existence for some time before the muscular atrophy is noticed, and before the conditions which are blamed as the cause come into effect.

There seems good reason to suppose that excessive muscular effort is sometimes the cause, or at least an exciting cause, of the disease. It is easy to understand that if the nerve cells have a tendency to degenerate, prolonged and excessive muscular effort, which throws a strain upon them, will be likely to excite or hasten the development of the degeneration. I have seen several cases which seemed to support this view. In one case, for example, the patient, a great pianist, was in the habit of playing the piano many hours each day. In another case, the patient was a blacksmith; in his case the over-use of the muscles of the hand and forearm which the effort of constantly grasping and raising a heavy hammer necessitated, was perhaps the exciting cause of the disease.

Traumatic injury to the back is sometimes blamed, and it is impossible to deny that concussion of the spinal cord and resulting injury to the delicate grey matter of the anterior horn (punctiform ecchymoses) may perhaps in some cases be the cause of the disease. But the cases in which progressive muscular atrophy can, with any degree of probability, be attributed to concussion of the cord or direct injury to the back are, so far as my information enables me to judge, exceedingly rare. Further, injury to a limb is occasionally followed by progressive muscular atrophy, and it has been supposed that in such cases the cord lesion is the result of an irritation, or perhaps an inflammation, which extends up the nerves from the seat of the injury to the spinal cord.

I need not say that the disease is often said to be the result of exposure to cold; possibly in some cases this cause is really effective. The disease sometimes develops (but this is, comparatively speaking, very rare) after syphilis. A well marked case of this kind came under my notice quite recently; but I doubt whether the syphilitic factor was more than a mere coincidence. It is possible that in many of the cases in which progressive muscular atrophy was thought to be the direct result of syphilis, the lesion which produced the muscular atrophy was situated in the peripheral nerves and not in the spinal cord. The Aran-Duchenne form of progressive muscular atrophy seems to be very rarely developed after an attack of one of the specific fevers. In this respect it contrasts remarkably with the peroneal type of muscular atrophy, which, as I shall afterwards point out, seems to be more closely related to this, the spinal, form of progressive muscular atrophy than to the idiopathic (myopathic) forms of muscular atrophy with which it is usually classified. Lead impregnation sometimes causes a diffuse muscular wasting which is readily mistaken for progressive muscular atrophy; possibly in rare cases lead poisoning is an actual cause of the disease.

In many cases, the conditions to which I have just referred as supposed causes are probably mere incidental factors, or at most exciting causes or aggravating conditions. In the present position of our knowledge, it is perhaps impossible to make a more precise statement respecting the etiology than this, viz., that the lesion seems to be a degeneration or chronic inflammation of the motor nerve cells of the spinal cord, and that anything which irritates, exhausts, or throws a strain on the nerve cells (which are predisposed to degenerate or which are already in a commencing state of degeneration) may probably act as an exciting cause of the degeneration, or hasten its progress once it is developed.

In connection with the etiology of the disease, I must not omit to mention the interesting fact that Roger (quoted by Grasset and Rauzier[1]), by injecting old cultures of the streptococcus of erysipelas into rabbits, produced a localised myelitis, the essential pathological feature of which was degeneration of the multipolar nerve cells of the anterior cornua of the spinal cord. This experimental lesion was attended with clinical symptoms identical with those of progressive muscular atrophy.

Clinical History.—In typical cases, progressive muscular atrophy is a very chronic disease. The onset is usually insidious and is unattended with fever or constitutional disturbance. In many cases, the atrophy has already made

[1] *Maladies du Système Nerveux*, page 622.

considerable advance before the patient becomes aware of its presence. This statement, of course, applies to non-professional persons, and especially to unobservant people in the lower ranks of society. Skilled observers (medical men) will be likely to detect the disease in its early stages; indeed medical men and medical students not unfrequently imagine that they are affected with progressive muscular atrophy. I shall return to this point when I come to speak of the diagnosis.

We have seen that according to some authorities the ordinary (spinal) form of progressive muscular atrophy and amyotrophic lateral sclerosis are mere varieties of the same disease. Bearing this opinion (with which I cannot as yet see my way to agree) in view, and admitting that in some cases of progressive muscular atrophy the crossed pyramidal tracts are sclerosed, let us consider the ordinary typical form of the disease, in which the lesion is, for clinical and practical purposes, confined to the anterior cornua of the spinal cord.

Muscular weakness in the hand (for the intrinsic muscles of the hand are in most cases first affected) is usually the first symptom which attracts attention.

In some (but they probably constitute a small proportion of the whole), the development of the disease is attended with myalgic or muscular pains. These myalgic pains may occur at any stage of the disease; they are more frequent in those cases which run an exceptionally rapid course. A more common symptom is a feeling of fatigue after exertion. True myalgic pains are much less common in progressive muscular atrophy than in some other affections, such as peripheral neuritis, in which muscular wasting is a prominent symptom.

In consequence of the muscular weakness, the patient finds a difficulty in performing certain movements. Thus, as Roberts graphically puts it:—'The tailor discovers that he cannot hold his needle, the shoemaker wonders he cannot thrust his awl; the mason finds his hammer, formerly a plaything in his hand, now too heavy for his utmost strength; the gentleman feels an awkwardness in handling his pen, in pulling out his pocket handkerchief, or in putting on his hat. One man discovered his ailment in thrusting on a horse's collar; another, a sportsman, in bringing the fowling-piece to his shoulder.'

Speaking generally, the loss of muscular power is proportionate to and coincident with, the amount of atrophy which is present. This is a general statement. Of course, the weakness is not absolutely equal to the atrophy, for before the nerve cells are completely destroyed, the functional activity of the muscular fibres with which they are connected is necessarily enfeebled; but speaking generally, the amount of atrophy is roughly proportionate to the degree of muscular weakness.

In the great proportion of cases, the muscular weakness and atrophy are first observed in the upper extremity. The muscles of the thumb (adductor longus pollicis and opponens pollicis) are usually first affected; then the muscles of the hypothenar eminence, and the interossei. In some cases, the muscles of the forearm, the deltoid, or some of the other muscles of the shoulder girdle or upper arm are first attacked; but this is exceptional. It is said that in rare cases the atrophy first develops in the muscles of the back or of the lower extremities. In many cases, the atrophy is already well advanced when the patient consults a doctor.

After the atrophy has developed to a certain degree on one side, it usually affects the corresponding muscles on the opposite side. But this is not by any means always the case. In many cases, the muscular weakness and atrophy are for a time limited to one arm or the muscles which attach the arm to the trunk; a very considerable degree of wasting may be produced in the arm which is first affected, before the muscles of the opposite limb are involved. In a small proportion of cases, the muscles of the lower extremities (the glutei, the muscles of the thigh, or the muscles below the knee) are first attacked. In some cases, the thoracic or trunk muscles are affected in the early stages of the disease; in rare cases, they are first involved. The upper part of the trapezius is very rarely affected, so seldom that Duchenne termed it *ultimum moriens*—the last muscle of the upper extremities and trunk to be attacked. The atrophy very seldom indeed affects the muscles of expression or the muscles of the tongue; but, as I have more than once stated, the motor nerve cells in the medulla oblongata are in many cases implicated in the later stages of the case, with the production of bulbar symptoms (muscular weakness and atrophy of the lips, tongue, pharynx, etc.).

The muscular weakness and atrophy gradually extend and involve other muscles, until finally almost all the muscles of the upper extremities and many of the muscles of the trunk may be implicated.

The muscular wasting is the most conspicuous—in fact, in many cases the only—alteration which is apparent. In the hand, the thenar and hypothenar eminences disappear, and depressions, due to the wasting of the interossei, are seen on the back of the hand between the metacarpal bones.

Atrophy of the interossei (the muscles of the forearm being unaffected) causes a peculiar alteration in the position of the fingers, to which the terms 'clawed hand,' '*main en griffe*,' have been given (see Plate LXXXV., figs. 3 and 4).

The manner in which this alteration in the position of the fingers is produced is as follows:—

The combined action of the internal and external interossei produces (as Duchenne was the first to demonstrate) a movement of the fingers in which the first phalanx is flexed on the metacarpus, and the second and third phalanges are kept extended; in other words, the action of the interossei is to place the fingers in the writing position. The direction of the tendon of the interossei perfectly explains this contradictory action upon the phalanges; in the first part of its course (from the metacarpal phalangeal articulation to the upper surface of the first phalanx), the tendon is directed obliquely from above downwards and from before backwards (see fig. 4).

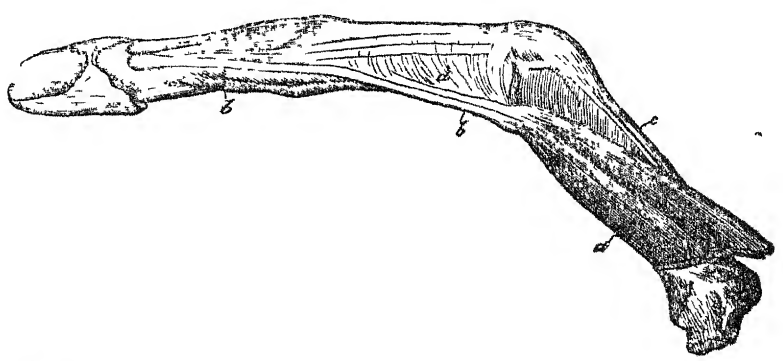


Fig. 4.—*Ring finger of the right hand, with its dorsal interosseous or adductor muscle.—(After Duchenne).*

(*a*) Dorsal interosseous or adductor muscle; (*bb*) phalangeal tendon of the dorsal interosseous; (*c*) tendon of the extensor communis; (*d*) aponeurotic expansion, which unites the phalangeal tendon of the interosseous with the tendon of the extensor.

There is therefore flexion of the phalanx on its metacarpal bone during contraction of the muscle. The second part of the tendon, which is united by an aponeurotic ex-

pansion to the tendon of the common extensor, is placed on the back of the phalangeal articulations; consequently the second and third phalanges are extended on the first phalanx during the contraction of the muscle.

Now, when the interossei are paralysed, the opponent muscles have full play; the result is extension of the first, and flexion of the second and third phalanges; in short, the hand assumes the '*bird-claw*' position.

The *main en griffe* or 'bird-claw' hand is not pathognomonic of progressive muscular atrophy; it merely indicates paralysis of the interossei, a condition which may, of course, be due to a lesion of the ulnar nerve. The appearance of the hand in the two cases (progressive muscular atrophy and paralysis due to a lesion of the ulnar nerve) is, however, somewhat different, a fact to which attention was first directed by Duchenne; in progressive muscular atrophy, all the fingers are equally affected, in paralysis of the ulnar nerve, the ring and middle fingers are more particularly involved.

The appearance which the forearm presents when its muscles are extensively atrophied is well seen in figs. 4 and 5, Plate LXXXV.

When the deltoid is affected, the roundness and plumpness of the shoulder disappears and the head of the humerus and bony prominences around the joint project conspicuously.

When the trunk muscles are affected in a marked degree, curvatures of various forms are apt to be produced Fig. 6, Plate LXXXV., represents a case in which the lumbar muscles were atrophied. In the erect position the back is curved so that a line drawn perpendicularly downwards from the shoulders falls right behind the sacrum; the pelvis is tilted forwards, and there is a compensatory backward curvature of the upper part of the spine, which entirely disappears when the patient assumes the sitting position, the back is then rounded and projects.

Fig. 7, Plate LXXXV, represents a case in which the abdominal muscles were atrophied. The back is bent backwards by the unopposed lumbar muscles, which were healthy; the abdomen is prominent, and a line drawn perpendicularly downwards from the shoulders falls well inside the sacrum.

In Plate LXXXIV. a typical case of advanced progressive muscular atrophy is represented. The patient was under my observation for many years, and was examined post mortem by Dr. Alexander Bruce and myself. The small muscles of the hand are completely wasted; and the muscles of the forearms and arms have almost entirely disappeared. The only movement which the patient could make with his upper limbs was to swing them about (in a feeble way) like a flail. The muscles of the thorax and back are markedly affected; the muscles of the neck are in some degree involved. The muscles of the lower extremities have almost entirely escaped. I may say in passing that in this very typical case the lesion was confined to the region of the anterior horn; there was absolutely no sclerosis of the crossed pyramidal tracts.

It is important to note that the atrophy not only involves the muscles, but also seems to affect the subcutaneous and fatty tissues; in advanced stages of progressive muscular atrophy the bones stand out like the bones of a skeleton; and the skin of the palms presents a wrinkled appearance.

The temperature of the wasted and atrophied limbs is usually considerably below the normal average.

In the earlier stages, the affected muscles are flaccid, more or less [illegible] and weak in proportion to the degree of atrophy which is present. In the advanced stages, the muscular tissue may have almost entirely disappeared. Pressure over the affected muscles does not cause pain. This is an important diagnostic point, for in some forms of peripheral neuritis in which muscular wasting is a prominent symptom—notably in alcoholic peripheral neuritis—muscular tenderness on pressure is a highly characteristic symptom.

Fibrillary twitchings or tremors, which consist in a momentary contraction of individual muscular fasciculi, can usually be seen in the muscles which are undergoing the atrophic process; they are, in fact, more frequent in progressive muscular atrophy than in any other disease. The skin covering the muscular fibre is suddenly raised and stretched, as if a thread were made tense beneath it. The patient may be conscious of a momentary quivering sensation in the affected part. I shall have more to say about these fibrillary tremors when I come to speak of the diagnosis.

The electrical condition of the affected muscles varies considerably in different cases. This is apparently due to the fact that the rapidity with which the atrophy and the nerve degeneration are developed, varies in different cases. In the early stages a 'simple diminution' to both forms of current may be the only apparent change; but in most cases, when the disease is well marked, the anodal closing contraction is equal to, or greater than, the cathodal closing contraction. There is, in short, an imperfect form of the reaction of degeneration. In progressive muscular atrophy some of the motor nerves and motor nerve endings are degenerated and destroyed, while some are healthy. Hence, when either the interrupted or the continuous current is applied to the partly atrophied and degenerated muscles and nerves, contractions are produced; for the healthy or comparatively healthy fibres which persist are capable of contracting to either form of current; but the contractions are less powerful, less forcible, than in health, for many of the muscular fibres are atrophied. But further, the constant current when applied directly to the atrophying muscles, stimulates not only the healthy motor nerve-endings, but the muscular (sarcous) substance of the muscular fibres which are partly, but not as yet completely, destroyed. The result is that the anodal closing contraction is as readily, or even more readily, produced than the cathodal closing contraction. It must, however, be stated that in some well marked cases of the disease, the order of the polar reactions is quite normal. In the more advanced stages of the disease, when the muscular fibres are entirely destroyed, it may be impossible to elicit muscular contractions with either form of current; but this is rarely the case, for some muscular fibres usually remain even in those muscles which appear to be completely wasted, to the naked eye. As a rule, the faradic irritability disappears before the galvanic irritability; and the electrical excitability of the nerves is, it is said, in some cases retained longer than the electrical excitability of the muscles.

The presence of fibrillary twitchings and of this imperfect form of the reaction of degeneration are most important features from a diagnostic point of view. Fibrillary twitchings and the reaction of degeneration are very rarely indeed observed in the myopathic forms of muscular atrophy.

In some cases of progressive muscular atrophy the mechanical and electrical excitability of some of the affected (atrophying) muscular fibres seems to be for a time increased. There seems, in short, to be a condition of irritable weakness. The affected muscles are more easily excited but at the same time more

easily fatigued and exhausted, both by voluntary and electrical stimuli, than in health.

The condition of the reflexes is also variable. When all the nerve cells in any segment are destroyed, the reflexes passing through the segment will of course be completely abolished. But the destruction of the nerve cells is rarely complete and in the early stages of the disease many nerve cells still remain. Hence, in the early stages of the disease the reflex impulses can still be elicited.

Suppose, for example, that one-third of the nerve cells in the affected part of the anterior horn of the spinal cord was degenerated, and one-third of the muscular fibres connected with the affected portion of grey matter consequently atrophied. In such a case, the reflex impulses would of course be unable to pass through the nerve cells which were degenerated, but could still pass through the nerve cells which remained healthy (see fig. 5).

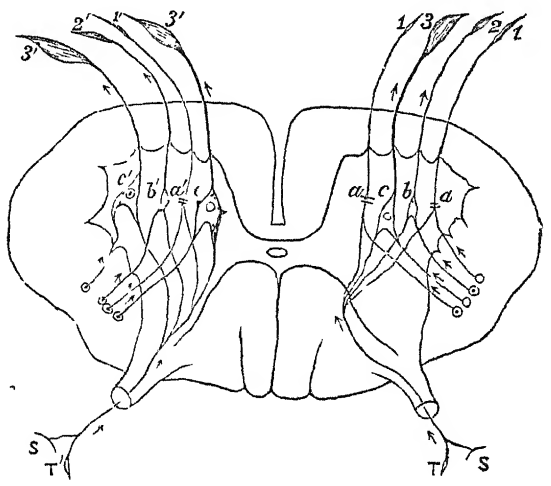


FIG. 5.—*Diagrammatic representation of the symptoms which result from slow destruction of the multipolar nerve cells of the anterior cornu.*

On the left side the disease is in an early stage. One nerve cell (a') is completely destroyed. Its muscular fibre (1') is completely atrophied Voluntary motor and reflex motor impulses are 'blocked' at the seat of the lesion (a'). One nerve cell (b) and its muscular fibre 2' are very much atrophied, but feeble motor and reflex impulses can still pass through the cell to the muscle. Two nerve cells c' c'' are healthy. Their muscular fibres are of normal bulk, and can be made to contract either by voluntary or reflex impulses.

On the right side the disease is much more advanced The muscular area is three fourths degenerated There is a total 'block' at a and a. This condition represents a late stage of progressive muscular atrophy. The atrophy of the muscular fibres is represented as *simple*.

But, as a matter of fact, the reflex movements are in many cases more interfered with than this statement would imply.

Further, it must of course be remembered, that it is only the reflexes which pass through the affected segments that are interfered with. Since the lesion does not as a rule involve the lumbar enlargement, the reflex movements in the lower limbs are not interrupted; in fact, in many cases they are exaggerated, for in many cases the crossed pyramidal tracts are sclerosed.

In typical and uncomplicated cases of progressive muscular atrophy, the sensory functions are practically intact. In some cases, the patient complains of numbness, deadness, or pins and needles in the affected part; but there is rarely any marked and definite anæsthesia, or any distinct impairment of the sensibility to heat or cold, or to pain.

The functions of the bladder and rectum are not interfered with. Of course, in the later stages of the disease, if the patient should become completely crippled and confined to bed (and this is the usual result in amyotrophic lateral sclerosis but a rare result in the ordinary variety of the disease) the bladder may become paralysed and bed-sores may be developed, as in any other advanced cord lesion.

The general health usually remains good throughout the whole course of the disease. As I have already told you, the fatty tissues of the body seem to waste and disappear, and the patients are usually thin and more or less emaciated The affected limbs are usually colder than normal. Sugar is occasionally present in the urine; this is, however, quite exceptional; the presence of glycosuria is suggestive of a lesion in the medulla oblongata; in cases of progressive muscular atrophy the presence of sugar in the urine is consequently a very unfavourable symptom.

Course.—The course of progressive muscular atrophy is usually very chronic; the disease generally lasts for years; but this is not invariable. Cases which run a subacute course are occasionally met with; cases have been recorded in which the total duration of the disease seems to have been less than eighteen months, but such cases are exceedingly rare.

Although the usual course of the disease is to advance and progress, the lesion not unfrequently seems to become arrested, more particularly after it has advanced up to a certain point. In some cases, death is the result of the extension of the lesion to the medulla oblongata and involvement of the cardiac and respiratory centres. In many cases the immediate cause of death is an attack of bronchitis. A trivial cold or slight bronchitis, which in an ordinary individual would cause little or no inconvenience, may easily prove fatal in those cases of progressive muscular atrophy in which the intercostal muscles or the diaphragm are paralysed and atrophied. In some cases, complications on the part of the bladder arise in the later periods, but this is not common. Death is sometimes due to the development of some intercurrent disease or complication, which does not directly depend upon the cord lesion.

Diagnosis—In typical and well developed cases, the diagnosis is easy. The recognition of progressive muscular atrophy must be based, partly upon the presence of certain (the positive) symptoms, viz., slowly developing muscular weakness and atrophy, the muscular weakness being in most cases directly proportionate to the muscular wasting; and partly upon the absence of other (the negative) symptoms, viz., the absence of well marked sensory disturbances and of any affection of the bladder or rectum.

The positive and negative symptoms and the very slow and gradual manner in which the disease is developed clearly show that there is a chronic lesion in the lower segment of the neuro-motor nerve apparatus or in the muscles themselves.

All acute lesions in this part of the neuro-motor apparatus (such, for example, as polomyelitis anterior acuta and the more typical and rapidly developed forms of peripheral neuritis) can be at once excluded.

The differential diagnosis of progressive muscular atrophy and of peripheral neuritis.—But in some cases of peripheral neuritis the onset is subacute, and in rare cases of progressive muscular atrophy the disease is developed more rapidly than is usually the case. In such cases, the diagnosis may be attended with more difficulty.

Inflammation of the peripheral nerves has, during the past few years, assumed a very important place in clinical medicine. We now know that peripheral neuritis is a common condition, and that it may be due to quite a number of different causes. Now, paralysis and muscular atrophy are conspicuous results

of peripheral neuritis, and in some cases, as for instance in alcoholic peripheral neuritis, the atrophy is widely distributed and may involve the small muscles of the hand which are so constantly affected in progressive muscular atrophy.

But notwithstanding these points of resemblance, the two conditions are readily distinguished. The mode of development and distribution of the paralysis and atrophy are essentially different in the two cases.

In most cases of peripheral neuritis, the onset is more rapid than in progressive muscular atrophy; the paralysis is the first event, and the muscular atrophy is secondary to it; the paralysis is more widely spread and (in the alcoholic form, and this is the most common variety and the one which is most likely to be mistaken for progressive muscular atrophy) the muscles of the leg and foot are more markedly affected than, or at least as much affected as, those of the forearm and hand. Further, in peripheral neuritis sensory symptoms (anæsthesia and hyperæsthesia) as usually prominent features in the clinical picture. A history of a definite cause can usually be elicited. The inflamed nerve trunks are tender on pressure, and in the alcoholic form—and this is a very characteristic symptom—muscular tenderness on pressure is usually well marked. Lastly, the paralysis and atrophy which results from peripheral neuritis tend to get well, and are in many cases completely recovered from, though recovery may be slow (several months, a year or even longer); while in progressive muscular atrophy the muscular weakness and atrophy tend to increase and extend.

The differential diagnosis of the spinal (Aran-Duchenne) type and of the idiopathic (myopathic) forms of progressive muscular atrophy will be better understood after I have described pseudo-hypertrophic paralysis and the allied forms of idiopathic muscular atrophy.

The differential diagnosis of the typical spinal (Aran-Duchenne) type of progressive muscular atrophy and of the peroneal type of progressive muscular atrophy (which is probably myelopathic rather than myopathic in nature) will also be subsequently considered.

The chief difficulty in diagnosis occurs in the earlier stages when the muscular wasting is localised and limited to the small muscles of the hand and thumb. But even in these cases a careful observer is usually able to come to a correct conclusion as to the nature of the case.

In cases of ulnar nerve paralysis, leprosy, amyotrophic lateral sclerosis, pachymeningitis cervicalis hypertrophica, tumours pressing upon the spinal cord and anterior nerve roots at the lower end of the cervical enlargement, and syringomyelia, the small muscles of the fingers and thumb may become atrophied, and a condition of the hand, which more or less closely resembles that characteristic of progressive muscular atrophy may be produced. But in each and every one of these diseases there are associated symptoms which unmistakeably show that the muscular wasting is not due to progressive muscular atrophy.

The differential diagnosis of progressive muscular atrophy in an early stage and paralysis due to a lesion of the ulnar nerve.—In progressive muscular atrophy, all the fingers are equally affected; but in ulnar nerve paralysis, the little and ring fingers are much more bent than the middle and forefinger, for the first and second interossei muscles, which are supplied by the median nerve, escape. In progressive muscular atrophy, sensation is not affected; but in ulnar nerve paralysis, there is anæsthesia on both sides of the little and on the ulnar side of the ring finger. In progressive muscular atrophy, there are no trophic alterations in the skin and nails; but in ulnar paralysis, trophic alterations in the skin and nails of the little finger are often present. Progressive muscular atrophy is slowly, while ulnar paralysis is usually rapidly developed. In ulnar paralysis, a history of injury to the ulnar nerve may be forthcoming, or a wound in the course of the nerve may be present.

In cases of bilateral paralysis of the ulnar nerve, the physician is apt to be thrown off his guard and to suppose that the case is one of progressive muscular atrophy, for bilateral paralysis of the ulnar nerve is very rare. A few years ago a case of this kind came under my own observation. Both hands presented the bird-claw condition; at first sight the case looked like one of progressive muscular atrophy. But on closer inspection the true nature of the case was apparent. The little and ring fingers were much more bent than the middle and forefingers; the characteristic anæsthesia was present; and on inquiry a history of injury was forthcoming. The patient had slipped and fallen on both elbows; a bilateral injury to the ulnar nerves had resulted. An interesting point in the case was the fact that the patient was the subject of urticaria scripta. I have noticed a tendency to inflammations of the peripheral nerves in other cases of urticaria scripta.

Leprosy.—In some other affections, the small muscles of the hand may become atrophied and wasted. Leprosy, a disease which is rarely seen in this country, is one of them. In anæsthetic leprosy, as in progressive muscular atrophy, the muscular atrophy and weakness are slowly and gradually developed, but the diagnosis presents no difficulty. In anæsthetic leprosy, the ulnar and other nerves in the forearm or upper arm are enlarged, in many cases, they can be felt as hard rigid cords, and they can in some cases be seen standing out in the forearm. Other symptoms and signs of anæsthetic leprosy (such as anæsthesia in patches, skin eruption, glandular enlargement in the groin, etc.) will probably be present. Further, the history (the locality in which the patient has lived and contracted the disease) affords corroborative evidence of the true nature of the case.

Amyotrophic lateral sclerosis.—This condition, which is now thought by some authorities to be merely a variety of progressive muscular atrophy, is easily distinguished from the ordinary form of progressive muscular atrophy. I will presently refer to its characteristic features in detail. The spastic condition in the lower extremities and the increase of the deep reflexes both in the lower and upper limbs clearly show that the pyramidal tracts are involved in a marked degree, and differentiate the condition from the ordinary form of progressive muscular atrophy.

Pachymeningitis cervicalis hypertrophica, and tumours which press upon the spinal cord in the lower cervical region.—These conditions are more likely to be confounded with amyotrophic lateral sclerosis than with the ordinary (uncomplicated) form of progressive muscular atrophy, from which they are readily distinguished. The chief points of distinction are, that in both affections (pachymeningitis cervicalis hypertrophica and tumours pressing upon the cervical region of the cord) symptoms indicative of implication of the posterior roots (pain and anæsthesia in the upper extremities) are usually prominent; and symptoms due to pressure upon the cord itself (weakness, paralysis, rigidity, spasm, exaggeration of the deep reflexes in the lower extremities) are often present. The wasting of the small muscles of the hand and the *main en griffe* (which may be present and which may suggest progressive muscular atrophy) are not the only symptoms—

unless indeed the anterior nerve roots in the lower cervical region are alone pressed upon and involved; but such limitation is very rare if it ever occurs.

Syringomyelia.—In this condition, in which cavities are developed in the centre of the cord, localised muscular atrophy is of frequent occurrence, for the region of the anterior horn is often invaded by the lesion. When the anterior cornu in the cervical region is implicated, the muscular wasting may closely simulate that due to progressive muscular atrophy. But in syringomyelia, other characteristic symptoms, notably loss of the temperature sensibility, and trophic lesions in the skin, nails or bones, are almost always present. Further, the distribution of the muscular wasting and the order of its development and spread are usually different from that which is present in progressive muscular atrophy.

Lead Poisoning.—In this condition, the cause of the muscular atrophy is usually clear enough. A distinct history of exposure to lead is usually forthcoming, and other symptoms characteristic of lead impregnation (blue line on the gums, colic, anæmia, etc.) are almost always present. Further, the muscular atrophy is usually different in the two cases; and in doubtful cases the practitioner can always fall back upon the therapeutic test—the effect of treatment. I have, however, seen at least one case of undoubted progressive muscular atrophy in which the patient had suffered from lead poisoning, and in which the plumbism was perhaps a cause (or possibly the chief cause) of the disease.

Localised lesions of the anterior horn of grey matter are occasionally developed in the course of locomotor ataxia, primary spastic paraplegia, and other chronic diseases of the spinal cord. But there is no difficulty in distinguishing the localised muscular atrophy which is produced in this way from that which is due to progressive muscular atrophy. In the great majority of cases, the muscular wasting is localised and limited to the lower extremities; further, it shows little or no tendency to progress and involve other muscles. This is a most important diagnostic point, for *the* essential feature of progressive muscular atrophy is the tendency to extend and to involve one muscle after another.

The diagnostic significance of fibrillary twitchings and tremors.—I have already stated that, although fibrillary twitchings and tremors are more frequent in progressive muscular atrophy than in any other disease, they are in no way pathognomonic or distinctive of that condition. In fact, quite the contrary. Fibrillary twitchings are by no means uncommon in neurasthenia and other functional conditions; they also occur in many organic affections of the spinal cord in which a subacute or chronic lesion involving the anterior cornual region is attended with muscular weakness, paralysis and atrophy—in traumatic myelitis (during the stage of recovery) and arthritic muscular atrophy, for example.

So far as my observation enables me to judge, fibrillary twitchings may result either from a condition of irritable weakness of the nerve cells—a functional condition—or from slow degeneration and destruction of the nerve cells—an organic condition.

Almost every one, I suppose, has experienced fibrillary twitchings in the eyelid; they are common enough, too, in other parts of the body. A layman who is affected with these fibrillary twitchings, and who knows nothing about progressive muscular atrophy, is rather amused than otherwise by them; but a doctor who observes these twitching in his own person sometimes at once jumps to the conclusion that he is going in for progressive muscular atrophy. The mental anxiety and depression which result from this idea are often very great. As a consequence, the general health, which was previously perhaps below par, becomes still further deteriorated. This imaginary form of progressive muscular atrophy is a doctor's disease. It is one of the imaginary diseases with which doctors and medical students are apt to be affected. The point which I wish to emphasise is, that the mere presence of fibrillary twitchings is no evidence of progressive muscular atrophy or indeed of any other serious disease of the nervous system. In the diagnosis of progressive muscular atrophy, and indeed of almost every other disease, the whole circumstances and facts of the case must be taken into account. Fibrillary twitchings *per se* are of little or no importance. It is very different if the fibrillary twitchings are associated with well marked and localised muscular atrophy.

It is important to remember that fibrillary tremors which are in most cases such a conspicuous feature of the Aran-Duchenne form of progressive muscular atrophy are very rarely indeed met with in the idiopathic (myopathic) forms of the disease. What I mean to say is this, that given a case of progressive muscular atrophy, the presence of fibrillary twitchings is an important diagnostic sign of the myelopathic as distinct from the myopathic form of the disease.

Prognosis.—Progressive muscular atrophy usually runs a very chronic course; but in some rare cases the duration of the disease is comparatively short; cases have been recorded in which the disease terminated within eighteen months from its commencement. Such a rapid course is, however, quite exceptional. The prognosis as regards duration is consequently, in most cases, fairly good.

The prognosis as regards complete recovery is very bad. The fact that the lesion is degenerative in character shows that there is an inherent tendency to decay in the affected nerve elements. The degenerative atrophy destroys the nerve cells, and so far as we know, nerve cells which have once been destroyed are never restored.

The prognosis as regards arrest is uncertain, and in most cases unfavourable. It is perfectly true that the morbid process is sometimes arrested; but in the majority of cases, the degeneration extends and gradually goes from bad to worse. In most cases, although temporary periods of apparent arrest may occur, there is no real arrest—simply a period of temporary quiescence. In other cases, after the lesion has advanced to a certain stage, a true arrest seems to occur. In the case which is represented in Plate LXXXIV., the patient lived for several years (the disease being in a static or arrested condition) after all the muscles of the upper extremities and shoulders and many muscles of the back and thorax had been completely destroyed. Arrest in the early stages (when, for instance, the atrophy is limited to the hand muscles) is in my experience very rare. Gowers thinks that arrest is more likely to occur in those cases in which the corresponding muscles on opposite sides of the body are simultaneously or almost simultaneously affected, than in those cases in which the atrophy is irregularly developed.

These are general statements. In trying to form a prognosis in any given individual case, the following are the more important points which have to be taken into account:—The length of time which the disease has existed; the rapidity with which

it appears to be progressing; the number of muscles which are affected; the degree of atrophy in the muscles which are affected; whether the respiratory muscles are involved or not; the presence or absence of bulbar symptoms; the age of the patient; the circumstances and surroundings of the patient; and the presence or absence of complications (phthisis, kidney disease, etc.).

One would naturally expect that the disease would be less amenable to treatment in old than in middle-aged people; and speaking generally this is the case. Degenerative processes are more common (and after they have commenced perhaps more apt to progress) in old than in young people; but the age of the patient is a very uncertain guide, for the mere fact that progressive muscular atrophy (a disease which is due to a degenerative process) occurs in a comparatively young person, shows that the normal vitality, so to speak, which the nerve cells ought to possess is not present.

When arrest does take place, it very often occurs, as I have already stated, after a large number of muscles, perhaps all of the muscles of both upper extremities, have become atrophied; in other words, after the majority of the motor nerve cells in the cervical enlargement of the cord are destroyed.

In every case of progressive muscular atrophy, symptoms indicative of involvement of the nerve nuclei in the medulla oblongata should be carefully looked for; bulbar symptoms are always of very grave significance. The presence of sugar in the urine, even without any other symptoms indicative of implication of the medulla oblongata, is unfavourable. In those cases in which bulbar symptoms are developed early, the course is usually very rapid, fortunately in most cases bulbar symptoms are not developed until the terminal stages of the disease.

When the intercostal muscles of the diaphragm are affected, even in a slight degree, the prognosis is bad; for in these cases a slight bronchitis may, in consequence of the difficulty in getting rid of the secretions which accumulate in the bronchi, prove fatal.

Paralysis of the bladder is another very unfavourable condition; fortunately it is very seldom developed until the terminal stages of the disease; and even then it is rare.

In estimating the prognosis, the presence or absence of associated lesions in other parts of the cord must of course be taken into account; in amyotrophic lateral sclerosis, for example, the prognosis is more unfavourable, both in respect to duration and probable arrest, than in the ordinary form of the disease in which the anterior cornual region is alone involved.

It is perhaps hardly necessary to say that the financial circumstances and surroundings of the patient materially modify the prognosis. One essential point in the treatment of the disease is to protect the patient from attacks of bronchitis and other pulmonary complications such as phthisis. Patients who are well off, and who are consequently well fed, well housed, well clothed, and well looked after generally, are, other things being equal, likely to survive longer than others who are less favourably situated in these respects.

Treatment.—Almost all observers are agreed that the treatment of progressive muscular atrophy is very unsatisfactory; this is only what we would expect considering that the morbid process is a degeneration which tends in most cases to progress from bad to worse. Gowers seems to differ from this view. In the last edition of his work on the spinal cord he makes the remarkable statement that 'in seven almost consecutive cases in middle life, the treatment (hypodermic injections of strychnine) has been followed by arrest within a month of its commencement, and the arrest has been permanent in all cases but one. In the senile cases,' he says, 'the treatment has failed, but in most of them the disease was in an advanced stage, and the lumbar cord had begun to suffer.' In some of the cases in which the result was prompt and distinct, strychnia given by the mouth had failed. He recommends that one injection should be given daily, at any convenient place. He gives one-hundredth of a grain of the nitrate of strychnia at first, rapidly increased to one-fortieth of a grain. It will be very remarkable if future observations confirm these results.

Arsenic is another remedy which is of undoubted value in degenerative nerve processes; I am satisfied that it is beneficial in some cases of progressive muscular atrophy. Nitrate of silver is probably also useful. Quinine, too, is perhaps also beneficial as a general tonic. So far as I know, these are the only drug remedies which are likely to have a beneficial influence upon the course of the disease; and so far as my experience enables me to judge—and this I fancy is the experience of almost every physician—their influence for good is very slight, at all events when given by the mouth. In most of the cases in which the disease becomes arrested, the arrest is probably due to a natural process rather than to the influence of drugs. It is impossible I think to predict in any individual case whether an arrest will take place or not.

In treating cases of progressive muscular atrophy, it is essential to attend to the condition of the general health, and to avoid everything which is likely to produce depression or to hasten the development of the degenerative process. The patient should be well fed, well housed, well clothed and carefully protected from cold and all depressing conditions, such as mental or emotional excitement. It is especially important to avoid all causes of muscular fatigue. A certain amount of muscular exercise is beneficial, for it is important to maintain the functional activity and healthy nutritive condition of the nerve cells and muscles which are as yet unaffected; but exercise which causes fatigue and throws a strain upon the nerve cells and muscles which are in process of degeneration should be avoided.

Fresh air and sunshine are eminently desirable; consequently, patients who are well off should be advised to spend the winter and early spring in the sunny South. Egypt, Tangiers and Algiers are perhaps the most suitable climates.

Local electricity and massage are, I think, useful; but they must be carefully and judiciously employed. Powerful electric currents are likely to do harm rather than good, and rough massage is injurious. The form of current (whether the faradic or galvanic) is not perhaps a matter of much importance. A current just sufficiently strong to produce muscular contractions is all that is necessary. I usually recommend a weak faradic current. I believe that local electricity, gentle massage, and muscular exercise, if judiciously and cautiously employed, are undoubtedly beneficial in some cases. They help, I think, to maintain the nutritive condition of the healthy (unaffected) muscular fibres and perhaps prevent the degenerative (atrophic) changes advancing as rapidly as they might otherwise do in the affected muscular fibres. But further, these means of local treatment encourage the patient to hope. He sees, feels, and realises that something definite and positive is being done, day by day, to arrest the development of the disease. He is

thereby enabled to maintain a cheerful and, to some extent at least, a hopeful tone of mind; and this of itself undoubtedly excites a beneficial influence upon the progress of the lesion. Or rather perhaps I should say that if the patient becomes despondent and gives up all hope, the course of the disease is apt to be influenced for the worse by the state of mental depression. In this, as in many other diseases, mental therapeutics play a most important part in the treatment. Speaking generally, a cheerful and hopeful condition of mind has a tonic and invigorating action upon the nutritive processes of the body; while a despondent and hopeless frame of mind has a most depressing and injurious influence upon these nutritive changes, and is apt, I think, to favour the development and to accelerate the course of many morbid processes. I do not wish to be misunderstood on this point. I do not mean to say that one should tell a patient who is suffering from progressive muscular atrophy that local electricity and massage, or indeed any other form of treatment, will cure him. That would be nothing less than arrant quackery. But, believing as I do that these remedies are in some cases beneficial in preventing the rapid development of the disease, I maintain that they should be employed, and that the patient should be encouraged to hope that in his case they may perhaps be, in some degree at least, beneficial.

The catalytic action of the constant current applied to the spine is probably also of some use; but it is very difficult to draw correct conclusions upon this point, and I speak with great reserve regarding it. The position which I take up is, that a weak constant current applied to the spine cannot possibly do any harm, and that although I am not personally convinced that it is actually beneficial, I do not feel justified in saying that it never does any good. It is possible I think that it may perhaps do good. Hence it is, I think, advisable to give the patient the benefit of the doubt. But I repeat that if the constant current is applied to the spine, a weak current only should be employed.

Throughout the course of the disease, and especially in those cases in which the respiratory muscles are involved, it is of the greatest importance to avoid everything which is likely to produce bronchial catarrh or any other respiratory complication. If the bladder should be affected, great care must be taken to prevent the development of septic cystitis. Fortunately in the great majority of cases of progressive muscular atrophy the risk of bladder and kidney complications is very slight. But it is essential to remember that they do sometimes occur.

During the last stages of the case, when the patient is confined to bed, care must of course be taken to prevent the development of bed-sores. The risk of bed-sores is greater in amyotrophic lateral sclerosis than in the ordinary form of progressive muscular atrophy.

In the later stages of uncomplicated cases of progressive muscular atrophy the duration depends in great part upon the way in which the patient is looked after and nursed.

In those cases in which there is a definite history of previous syphilis, iodide of potassium and mercury should of course be tried.

DESCRIPTION OF PLATE LXXXV. Progressive Muscular Atrophy.

Fig. 1.—Transverse section through the anterior horn of the spinal cord in a case of progressive muscular atrophy.

The anterior horn of grey matter is shrunken. The nerve cells have almost entirely disappeared; one cell of normal size and one or two atrophied cells only remain. The blood vessels are much dilated. Under a high power the grey matter of the anterior horn is found to be sclerosed; numerous small corpuscles (leucocytes), which are probably indicative of the inflammatory character of the lesion, are scattered through the grey matter and especially around the dilated vessel. The letter *a* points to the only large nerve cells in the section. The letter *b* points to dilated blood vessels.

Fig. 2.—Transverse section through the anterior horn of a healthy spinal cord, for comparison with Fig. 1. (The nerve cells in this figure are too large.)

Figs. 3, 4 and 5.—Hands in cases of Progressive Muscular Atrophy.—(*After Duchenne.*)

Fig. 6.—Atrophy of the lumbar muscles in Progressive Muscular Atrophy.—(*After Duchenne.*)

Fig. 7.—Atrophy of the abdominal muscles in Progressive Muscular Atrophy.—(*After Duchenne.*)

Fig. 8.—Back view of the case of Progressive Muscular Atrophy represented in Plate LXXXIV

THE PROGRESSIVE MUSCULAR DYSTROPHIES

IN this article I propose to direct attention to those forms of muscular atrophy which, so far as our present knowledge and methods of investigation enable us to judge, are of *myopathic* origin, i.e. due to a lesion in the muscles themselves.

The subject is a difficult and complicated one, for several of the forms of myopathic muscular atrophy to which I am about to refer have only been recently differentiated, and there is still some uncertainty as to their true pathology and as to the relationship which they bear to one another. Further, cases of myopathic atrophy (the pseudo-hypertrophic type alone excepted) are, in this country at all events, rare, and the opportunities of studying them seldom occur.

The most striking clinical feature of the myopathic forms of progressive muscular atrophy, as of the spinal form of progressive muscular atrophy, is a slow, gradual and (usually) progressive muscular wasting, which is manifested externally and perceived by the patient as a gradual and progressive loss of motor power.

Now, muscular atrophy may of course be due to a lesion in any part of the lower division of the neuro-motor nerve apparatus (anterior horn of the spinal cord, anterior nerve-roots, peripheral motor nerves, or motor nerve-endings in the muscles), or to a lesion of the muscles themselves; that is to say, to a lesion (1) in the anterior horn of the spinal cord, (2) in the nerve tract which passes from the anterior horn to the muscles, or (3) in the muscles.

Acute destruction of the multipolar nerve cells in the anterior horn of the spinal cord is, as every one knows, followed by rapid and marked muscular atrophy, and acute destruction of a motor peripheral nerve produces the same result.

The slow and gradual destruction of the multipolar nerve cells (the trophic centres) in the spinal cord, which is the pathological substratum of the Aran-Duchenne type of progressive muscular atrophy, is attended with a slow and gradual muscular atrophy. Slow and gradual destruction of the motor fibres of the peripheral nerves will necessarily be followed by the same result. But slow and gradual destruction of the motor nerve fibres without any corresponding affection of the sensory nerve fibres is very rarely met with as a primary condition. Destruction and degeneration of the peripheral nerves, the result of peripheral neuritis, is common enough; but in the great majority of cases, peripheral neuritis runs an acute or subacute course; and it is only in quite exceptional cases of peripheral neuritis that the motor nerve fibres are alone implicated. Except in those cases in which degenerative and atrophic changes in the nerve fibres are secondary to a slow and gradual destruction of the nerve cells in the anterior horn of the spinal cord (their trophic centres), slow and gradual destruction and degeneration of the motor, apart from the sensory, fibres of the peripheral nerves very rarely indeed occurs.

A slowly developed and progressive muscular atrophy, without associated sensory symptoms, is consequently very rarely the result of a primary lesion of the peripheral nerves, that is to say, it is very rarely neuropathic. There is indeed one form of progressive muscular atrophy which is supposed by some authorities to be due to this cause—I refer to the peroneal type of the disease. But whether in that affection the lesion is actually situated in the peripheral nerves is, as yet, by no means certain. I shall refer to this question in more detail presently.

From these considerations, it will be obvious that a slowly developed progressive muscular atrophy, which is entirely unassociated with sensory symptoms, is in the great majority of cases either myelopatic or myopatic, i. e. due to a lesion in the spinal cord or the muscles themselves. As a matter of fact, most of the forms of progressive muscular atrophy which I propose to consider in this article are, so far as our present methods of investigation enable us to judge, of myopathic origin. This statement is based upon the results of histological examination; for up to the present time no definite and constant lesions have been detected in these cases, either in the spinal cord or in the peripheral nerves. It is true that in individual instances such lesions have been described, but in the great majority of cases which have been carefully examined by competent observers, working with modern methods, the spinal cord and peripheral nerves have been found to be absolutely healthy.

But granting this, it is not impossible to conceive—and the passage which I will presently quote from Erb gives some support to this view—that the *muscular* changes, which, so far as our present means of examination enable us to judge, constitute the primary lesion, may be the result of changes in the trophic centres for the muscles (multipolar nerve cells of the anterior cornua), which are too delicate to be recognised by our present methods of investigation. The healthy functional and structural condition of the muscular fibres of course depends upon (is governed by) the trophic nerve cells. It is not unreasonable, I think, to suppose that an altered condition of these trophic centres—a change which is, as we term it, functional and unattended with any obvious structural modifications, or at all events with any alterations which we can at present recognise—may exist as the peculiar mode of function in certain individuals (the subjects of myopathic atrophy) and may, in them, lead to the altered state of muscular nutrition which is the cause of the atrophy and hypertrophy of the muscular fibres and of the increase of the interstitial fibrous tissue which seems to be the primary pathological condition. The statement of Erb which seems to me to give some support to this view is as follows:—

'On the other hand, the results of the examination of the nervous system have, up to the present, been almost wholly negative. Leaving out of account Lichtheim's case and the older cases of pseudo-hypertrophy, we have had recently a series of exact records from Fr. Schultze, Landouzy, Déjerine, P. Marie, Dreschfeld, Westphal, and Singer, and neither in the spinal cord

nor in the peripheral nerves have any noticeable changes been observed. In accordance with these records, we should be entitled to view this dystrophy as a disease limited to the muscle-substance, and as a truly primary myopathy, were it not that some facts have come out which warn us to exercise great caution in this direction. Heubner's case deserves special mention. Though an undoubted case of dystrophy, he found there was extensive atrophy of the large cells in the anterior horns of grey matter. Frohmaier has a similar case with the changes in it less marked. In this new light the more trifling alterations observed by Singer and the older observations in pseudo-hypertrophic cases of L. Clarke, Gowers, Kestevan, Bramwell, and J. Ross, gain a certain significance. But in the meantime we must say this, that in progressive muscular dystrophy in its various forms, the nervous system must be considered to be, as a rule, and for our present methods of investigation, normal.

This is the place in which to say a little about the proper nature, pathogenesis, and exact seat of the lesion. It is not necessary to prove further that it is neither a simple atrophy of the muscles nor an inflammatory affection with its consequences; there is unquestionably a more complicated disturbance of nutrition, regarding the nature of which, for the present, I would rather not express a definite opinion.

Pathological anatomy has led many to consider it simply as a local muscular affection, quite independent of the central nervous system, a pure myopathy. But a good deal of doubt has been expressed (for example, by Knoll) regarding this view, and I myself, in my earlier work, brought forward some reasons which prevented me from accepting it without more inquiry. A much larger experience, a good deal of consideration given to the subject, and most of all the results of the previously mentioned autopsies have confirmed me in my scruples.

The considerations which weigh with me are various. The muscles depend for their nutrition to a very large extent on trophic nerve centres; the localisation of this atrophy frequently follows in a noticeable way the exact course of the nerves in a plexus, or the disposition of the centres in the central organ, and occasionally we find a case of spinal amyotrophy (Strumpell's case) presenting an almost exactly similar arrangement. Hereditary influence is of great importance; mental aberrations are common among the patients, and other neuroses frequently occur in their families. Further, even in the undoubtedly spinal cases, such as acute anterior poliomyelitis, similar morbid changes (hypertrophy, proliferation of nuclei, division of the fibres) both in the muscles and connective tissue have been pointed out by W. Muller, Déjerine-Huet, Joffroy-Achard, and Hitzig. In pseudo-hypertrophic cases, malformations and changes of a minor kind in the spinal cord have been met with. When I consider these facts, and bear in mind further the results of Heubner's and Frohmaier's observations, I cannot avoid the suspicion that after all the affection may be dependent on the nervous system. It is tempting to suppose, as I formerly expressed it, that we have to do with a kind of trophoneurosis, having its origin in the trophic centres of the cord —a disturbance of the function of these centres which finds its expression in the very complicated muscle changes of the disease. While on this supposition there are, as a rule, no coarse nerve changes, now and then, and after the affection has lasted a long time or been very intense, such a change does become visible.

The idea is inevitable that if something like this is the case the relations between dystrophy and spinal amyotrophy will turn out again in the end to be close and intimate. The latter would represent an affection of the trophic centres that from the very first is a distinct coarse anatomical lesion taking effect in a degenerative atrophy of the muscles with fibrillar twitchings, reaction of degeneration, etc.; the former at the outset would be merely a functional disturbance of these centres, conditioned probably by different causes, and expressing itself as muscular dystrophy with all its characteristic symptoms. At the same time, there would remain the possibility that even this merely functional disturbance might in the long run become associated with a coarse lesion of the centres. Many things about these affections would agree very well with such a supposition, among them the occasional occurrence of the reaction of degeneration in dystrophic cases and the occasional initial localisation of spinal amyotrophy in the shoulder and trunk. But I will not spin out this discussion to any greater length; the whole question is by no means yet ready for decision, and the future alone can lift the veil and reveal the finer processes that as yet lie hid from us.'[1]

[1] *Clinical Lectures by German Authors*, Third Series (Sydenham Society's Translation), page 261.

The chief facts in favour of the myopatic origin of the lesion are:—(1) The absence of any definite and constant changes in the spinal cord or peripheral nerves; (2) The fact that the muscular changes (atrophy and hypertrophy) do not, as a rule, seem to correspond in their distribution to the areas of distribution of the spinal segments, nerve roots or peripheral nerves; and (3) The interesting fact pointed out by Babinski and Ohanoff (quoted by Grasset and Rauzier, page 643) that the muscular atrophy corresponds in its distribution to the 'embryonic areas' of the muscles.

Quite recently Von Babes has described certain alterations in the nerve terminations in the muscles in pseudo-hypertrophic paralysis and juvenile muscular atrophy, viz., (1) a defective development of the nerve-ending and of the fibre which gives rise to it; (2) a degeneration (dissolution) of the already formed end-plate.[1] It will be extremely interesting to see whether these very suggestive observations are confirmed by independent investigation.

In some cases of pseudo-hypertrophic paralysis (and perhaps in the other varieties of myopathic muscular atrophy) there seems to be a tendency to a defect in development of the spinal cord. Now, if this is a fact (and I will refer to it more in de-

[1] The following abstract of Von Babes' paper was published in the Epitome of the *British Medical Journal*, Oct. 6, 1894:—

THE NERVES IN PSEUDO-HYPERTROPHIC PARALYSIS

Von Babes (*La Roumaine Médicale*, August 1894) describes a new appearance (pathological) of the nerve terminations in this disease. Peripheral nerve terminations normally end in free blunt points or arborisations, and the recent discoveries with the Golgi method had served to emphasise this distinction. The author, in the course of examination of nerve endings in muscle and connective tissue, came across appearances which seem to differ essentially from the idea that nerve filaments necessarily have terminations in the strictest sense. In two cases—one of so called primary juvenile muscular atrophy, and the other of infantile pseudo hypertrophic paralysis —the following were found. One specimen of the pseudo hypertrophic gastrocnemius with its connective tissue (fascia) was studied with Ranvier-Lowitt's gold chloride method, which stains the neuro muscular end plates. A remarkable change was observed; the motor fibre going to the muscle was in the first place remarkably thinned and attenuated, though preserving its myelin sheath, the latter being poor in cells and therefore presumably not undergoing degeneration. Its termination, where it abutted against the muscle fibre, was by a small conical enlargement, pale, and either simple or giving rise to a few very short and extremely fine filaments, which radiated from it star-wise. The terminal plate was thus of small size (atrophied or non-developed) and much simplified. [This appearance is indeed like those described by Ramon y Cajal in the growing points of the motor fibres of the spinal cord of the chick—'points d'accroisement'—in which case it would serve to show that the muscular nerve ending is yet in a very rudimentary condition in the disease.] Other specimens showed not only the atrophied (diminished) condition of the end plate, but the presence of small fusiform cells about this region, such as had been shown to be present in the experimental degeneration (Wallerian) induced in the nerve terminations by sections of the nerve trunk. This would seem to indicate that a veritable process of degeneration (dissolution) was going on. In two specimens (prepared by the isolation and teasing method) a single thick medullated fibre (4μ diameter) has been seen to divide, the two branches sweeping round in semicircular fashion to reunite into a distinct ring—a condition never observed before. From each segment of this ring or loop a fine medullated branch was given off, which, after winding spirally round the parent branch for some distance, left it to end freely; one of these shortly after ending in contact with a muscle fibre, the myelin sheath stopping short just before. The other fibre passed into the connective tissue, ending freely in an oval termination, within which a fibre formed a knot or swelling, and a number of sinuous twists without losing its continuity. This, the author thinks, is comparable to sensory termination of the nerve; in any case, it is not motor. This double termination of a single medullated fibre, namely, by a motor and a sensory ending in the muscular tissue, the author is inclined to look upon as possibly normal, and which had before been overlooked owing to the extent and size of the nerve loop which gives rise to it. If confirmed, his conclusions would seem to show that the pathological conditions underlying the nerve ends in juvenile muscular atrophy and pseudo-hypertrophy are of the non-developmental type, that is (1) a defective development of the motor ending and of the fibre which gives rise to it, and (2) a degeneration (dissolution) of the already formed end plate, the two appearances being apparently distinct; while on the other hand, the subdivision of a single muscular nerve into a sensory and a motor filament lands us in a new region of nerve function altogether.

tail when I come to describe pseudo-hypertrophic paralysis, it is of great importance and suggests that the pathology of the so-called myopathic forms of progressive muscular atrophy should, as Erb has suggested, be founded on a much broader and more extensive basis than the purely myopathic origin of the disease would suppose.

The chief points of pathological and clinical difference between the myelopathic and the myopathic forms of progressive muscular atrophy.

Pathological differences. The essential pathological point of difference or distinction between the myelopathic form of progressive muscular atrophy (represented by the Aran-Duchenne type of the disease) and the myopathic forms (such as pseudo-hypertrophic paralysis, the juvenile form of progressive muscular atrophy of Erb, the facio-scapulo-humeral type of Landouzy and Déjerine) is that, in the former, the muscular atrophy is due to a lesion of nerve cells in the anterior horn of the spinal cord; whereas, in the latter, there is no discoverable lesion, either in the spinal cord or peripheral nerves. In the present state of our knowledge, then, the myopathic atrophy seems to depend upon a lesion which has its starting point in the muscles themselves.

Another point of pathological difference between the two forms seem to be this, that in the myelopathic form the affected muscles and muscular fibres simply waste, but in the myopathic forms the affected muscles almost invariably (probably always as a matter of fact at some period or other of their course) contain enlarged or hypertrophied muscular fibres. Whether this distinction is absolute or not is perhaps as yet uncertain; probably it is not absolute, but so far as our present knowledge enables us to judge, it is a point of great importance. And here I may say that if hypertrophied muscular fibres are occasionally met with in cases in which the nerve cells in the anterior horn of the spinal cord are undoubtedly affected, it lends some support to the view that the myopathic muscular atrophies are in reality myelopathic (see below). This does not of course necessarily follow. It is possible that in some of these cases the lesion is a mixed one. What I mean to say is this, that in some cases of progressive muscular atrophy it is perhaps possible that the myelopathic and myopathic forms of atrophy may be combined. Further, it has been suggested, though I cannot agree with this supposition, that the changes in the nerve cells are the result of the changes in the muscle, in other words, that the myopathic atrophy is the first event, and the atrophy and degeneration in the nerve cells of the anterior cornua a secondary result of that atrophy. There are, in short, various ways of looking at the facts. In the present state of our knowledge the question must, I think, be left an open one.

According to the Erb, the histological changes in the muscles which are characteristic of the myopathic forms of progressive muscular atrophy are as follows:—

'First of all there is very considerable hypertrophy of the fibres, to as much as three or four times the normal.[1] Then there are all possible degrees of atrophy; rounding of the fibres till they are circular in form; increase of the nuclei both at the edge and in the interior; the formation of slits and the division of the fibres into two or more finger-like processes; vacuolation, sometimes only here and there, sometimes to a greater extent; faint transverse and pronounced longitudinal fibrils. On the other hand, there is no fatty or wax-like degeneration of the fibres.

'The changes in the connective tissue are increase and overgrowth, slight to begin with, more abundant later on. There are firm broad strands lying between the muscle-fibres, with abundant nuclei and thickened multinucleated vessel-walls. Besides these changes there is sooner or later more or less of a deposit of fat, which may go on to distinct lipomatosis.'[1] (See fig. 6.)

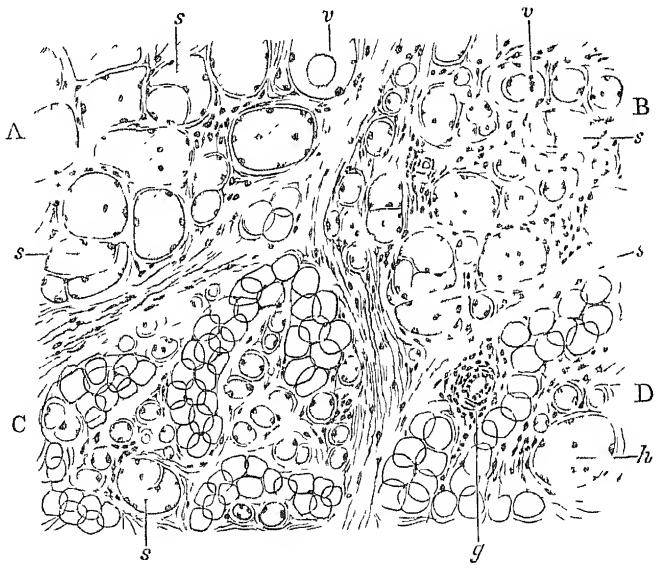


FIG. 6.—*Transverse section of muscle in progressive muscular dystrophy, made by combining four different sections from as many different cases.—(After Erb)*

A From the hypertrophied deltoid of a typical juvenile case; showing almost everywhere very much enlarged fibres with increase in the nuclei, slitting (*s*), and vacuolation (*v*); slight increase in connective tissue with abundant nuclei

B From the atrophied biceps of an intermediate case (juvenile? pseudo-hypertrophic?) showing muscle fibres of very different sizes, with great proliferation of the nuclei, abundant slitting (*s*), and here and there vacuolation (*v*), connective tissue very much overgrown and with numerous nuclei; no fat deposit.

C From the enlarged serratus magnus of a pseudo hypertrophic case (our third case) Muscle fibres mostly atrophied, here and there enlarged and slit (*s*); abundant firm connective tissue; large deposits of fat cells.

D. From the very atrophied biceps of a juvenile case, showing little else than adipose tissue lying among stout bands of connective tissue, the vessels of the latter very much thickened (*g*); small insulated patches of muscle-fibre in some places still very much enlarged (*h*) with numerous nuclei.

Clinical differences. The chief points of clinical difference and distinction between the myelopathic and myopathic atrophies are not perhaps quite so sharply and accurately defined as these pathological observations would seem to show; for according to some observers fibrillary twitchings and the reaction of degeneration, which Erb emphatically maintains are conclusive of the myelopathic form, are occasionally, though quite exceptionally, also present in the myopathic form. If subsequent observation should show that these statements are well founded—and I can speak positively as to the presence of fibrillary tremors, for in two cases of myopathic atrophy which have come under my observation the fibrillary tremors were extremely well marked—the fact may perhaps be explained, by supposing, either that (in these exceptional cases) there is a disordered or diseased condition of the nerve cells of the spinal cord, or that the lesion is a mixed one.

Speaking generally, the points of clinical distinction between

[1] 'I know very well that, according to the observations of Auerbach and of Oppenheim and Siemerling, the existence of this hypertrophy *intra vitam*, at least in the fragments of muscle excised from the living subject, has been called in question. But as it is present in exactly the same way in muscles taken from the dead body, and as we can decidedly infer from the marked proliferation of nuclei and division of the fibres that there is some process of overgrowth going on in the muscle, I should like in the meantime to hold by the real existence of this hypertrophy, though its exact degree may possibly be modified and conditioned by the method of preparation. Knoll's work has thrown some direct light on this point, and leads to the same conclusion.'

[1] *Clinical Lectures by German Authors*, Third Series (Sydenham Society's Translation), page 258.

the myelopathic and myopathic forms of progressive muscular atrophy are as follows:—

1. Fibrillary twitchings, which are such a characteristic and conspicuous feature in the great majority of cases of myelopathic atrophy (the Aran-Duchenne type and amyotrophic lateral sclerosis) are very rarely observed, in a characteristic and conspicuous form, in the myopathic forms.

2. The reaction of degeneration, which in its imperfectly developed form is usually a characteristic feature of the advanced stages of the Aran-Duchenne type of progressive muscular atrophy, is very rarely met with in the myopathic forms.

3. The small muscles of the hand, fingers and thumb, which are (? always) atrophied in the Aran-Duchenne type, and which, in the great majority of cases, are the muscles which are first affected in that, the myelopathic, form of progressive muscular atrophy, are rarely affected, until at all events, the later stages of the myopathic forms, though this may undoubtedly occur. It must, however, be remembered that in the later stages of the myopathic forms of muscular atrophy all the muscles, or practically all, may be atrophied.

4. True or false hypertrophy of the muscles is never met with in cases of myelopathic atrophy, but is very frequently developed in the myopathic forms of the disease. In pseudo-hypertrophic paralysis, the pseudo-hypertrophy of the muscles is one of the most striking clinical characteristics; indeed, from a diagnostic point of view, the pseudo-hypertrophy of the calf muscles is the most characteristic feature. In short, in the myelopathic (Aran-Duchenne) type of progressive muscular atrophy, the distal muscles of the limbs are usually first affected; while, in the myopathic forms of the disease, the proximal muscles of the limbs are usually first involved. In some cases of myopathic muscular atrophy the muscles of the back are first or very early involved. The frequency of this mode of development in the pseudo-hypertrophic type has I think in all probability been under-estimated.

5. The myelopathic form of progressive muscular atrophy is very rarely hereditary; whereas, the myopathic forms are very strongly hereditary. Cases of the Aran-Duchenne type are almost always solitary, in other words, two or more cases of this disease are very rarely met with in the same family (brothers and sisters), or in the same generation (cousins); but it is quite common, in fact (so far as our present knowledge enables us to judge) the rule for more than one case of myopathic atrophy to be found in the same family or in collaterals of the same generation. I may, however, take this opportunity of stating that solitary cases of the myopathic forms of progressive muscular atrophy are probably more common than is usually supposed. As Erb has pointed out, the disease must have a beginning some time; and isolated cases are by no means uncommon. Nevertheless, the hereditary and family tendency is a very striking point of difference between the myopathic and the myelopathic forms.

6. The age at which the disease develops in the two cases is different. The myelopathic form is essentially a disease of the adult and of the degenerative period of life; while the myopathic forms are usually developed during childhood, youth and early adult life, though in exceptional cases the disease may be developed later.

7. The order of development of the muscular atrophy is different in the two cases. In the great majority of cases of myelopathic atrophy (the Aran-Duchenne type), the small muscles of the hand are first affected; the disease very rarely commences in the lower extremities or in the muscles of the back, and the facial muscles are seldom if ever involved. Whereas, in the myelopathic forms of atrophy, the small muscles of the hand almost always escape until the later stages of the disease; the atrophy often commences in the muscles of the lower extremities or sometimes in the muscles of the back (in the pseudo-hypertrophic form of the disease these are the usual starting points), and occasionally in the muscles of the face.

8 In the myopathic forms of muscular atrophy, the tendon reflexes are diminished or abolished, never increased; whereas in the Aran-Duchenne type of the disease, the knee-jerks are often exaggerated and ankle-clonus is not unfrequently present

9. In the Aran-Duchenne type of progressive muscular atrophy, 'bulbar symptoms' are sometimes developed, for the lesion may extend to the medulla oblongata; but in the myopathic forms of muscular atrophy, bulbar symptoms do not occur.

The characteristic features of the myopathic forms of progressive muscular atrophy.—To sum up, the chief characteristics of the myopathic form of progressive muscular atrophy are as follows:—

1. The slow and gradual development of muscular atrophy and muscular weakness proportionate to that atrophy.

2. The progressive character of the muscular atrophy.

3. The development, though this is not invariable or at all events not always observable, of muscular enlargement, which in some cases appears to be a true and in other cases a false or pseudo-hypertrophy.

4. The absence of fibrillary twitchings.

5. The absence of the reaction of degeneration.

6. The strong hereditary tendency which the disease presents.

7. The strong tendency which the disease has to affect several members of the same family.

8. The fact that in the great majority of cases the disease develops during childhood, youth and early adult life.

9. The absence of any affection of the sphincters of the bladder and rectum.

10. The fact that if the deep reflexes are altered, they are always diminished or abolished, never exaggerated.

11. The entire absence of sensory symptoms.

12. The absence of any lesion which can be demonstrated by modern methods of investigation in the spinal cord, peripheral nerves, or (?) motor nerve-endings.

13. The presence in the affected muscles of enlarged (hypertrophied) muscular fibres.

As I have already pointed out, there is considerable difference of opinion amongst different observers as to the constancy of some of these characteristics. Some authorities, for example, state—and with them I agree—that in some exceptional cases of myopathic atrophy, fibrillary tremors occur; others say that the reaction of degeneration is sometimes developed in some of the affected muscles. Further, it is doubtful whether the presence of enlarged (hypertrophied) muscular fibres is absolutely pathognomonic.

The muscular atrophy and muscular enlargement (either true or false) which constitute the essential clinical features of the various forms of myopathic muscular atrophy, may develop in a different order and be distributed in a different manner in individual cases of the disease. Several forms or types (based

upon the order in which the muscular atrophy is developed and the manner in which the muscular atrophy and pseudo-hypertrophy are distributed) have been described. Until quite recently these different varieties or types were considered to be different diseases; but recent observations seem to show that many of them, at all events, are mere modifications or varieties of one fundamental or primary disease—the myopathic form of progressive muscular atrophy or progressive muscular dystrophy, as it has been termed.

The facts which Erb has advanced in favour of the view that the different types of myopathic muscular atrophy are modifications of one and the same disease are in my judgment conclusive. He says:—

'They all agree in the slow and insidious development of the disease, with very frequently hereditary or family influences at work; in the general wasting of many of the muscles combined with increase in the size of others; very notably in the localisation of the affection, in that almost invariably they are exactly the same muscles in the different cases that atrophy on the one hand, and exactly the same that become hyertrophied on the other; in the way in which this localising takes place in the trunk, shoulder girdle, and loins, and in the proximal ends of the limbs, the distal ends remaining free for a long time; and in the peculiar changes which are then brought about in the form and movements of the body, the attitude, and gait. They agree further in the condition of the muscles, as ascertained by percussion and palpation, in the effects of electrical stimulation, particularly in the absence of the reaction of degeneration, in the fact that there are no fibrillar twitchings, and in the gradual disappearance of tendon reflexes. Finally, in all of them the various forms of skin sensibility, the special senses, the muscular sense are absolutely normal, the sphincters are unaffected; the brain and organs of special sense, and all the internal organs, are quite normal.

'Thus in all the forms the outline of the features is the same, and yet there are certain differences which cannot be overlooked. These are as follows: Some of the cases appear to be independent of hereditary influences; sometimes the process begins in earliest childhood, sometimes in youth or at puberty, sometimes even later. In some cases it makes its appearance first in the loins and lower extremities; in others in the shoulders and upper extremities; at times even in the face. The rules of localisation are often set aside, the muscles of the forearm and small muscles of the hand being sometimes attacked, and muscles which, as a rule, are affected, being sometimes exempt. The degree of muscular hypertrophy may vary extremely, at times being quite unnoticeable, or limited to a few muscles, at times extended over a wide area, and present in a very marked degree. Further, this hypertrophy appears in some of the cases to be a true hypertrophy, depending on actual increase in volume of the muscle substance, and in others to be false, caused by a deposit of fat or lipomatosis. Lastly, the rate at which the disease advances, and the way in which, towards the close, all the muscles of the body may be affected, are very different in the individual cases.

'The longer I have occupied myself with the question, and the wider my experience of these forms has grown, the more has the conviction forced itself upon me that they all present one and the same disease. I am satisfied that, while in subordinate features such as the time and rate of development, the initial localisation, quantitative differences in the individual symptoms, particularly as regards the amount of hypertrophy, they may differ from one another, yet in all essential points they thoroughly agree. The proof of this clinical unity of those forms must, in the first instance, of course, be deduced from clinical material, but, from the number of my own cases and from a record on the part of others which has gradually grown to be very large, we have no difficulty about that.

'First of all we must establish the fact that the separate forms agree with one another in the following particulars:—The development and the localisation of both the atrophy and the hypertrophy in the muscles; the condition of the latter, as ascertained by inspection and palpation, by their mechanical and by their electrical reaction; and, lastly, the absence of all other symptoms.

'But still more convincing evidence is given by the cases, and they are not so very rare, which may be looked upon as transitional varieties between those individual types—cases of one form, in which you meet with certain features which you have learned to consider as properly belonging only to another form. For example, there have been lately observed several cases, both of the juvenile and of the pseudo-hypertrophic form, in which the muscles of the face have become involved (as in the second case which I showed you); or you may see the infantile form, beginning with pronounced facial atrophy, developing, as regards the rest of the body, at one time the juvenile type, at another time the pseudo-hypertrophic type; or you may observe the lower half of the body take on the distinct pseudo-hypertrophic type, while the upper half is an example of simple atrophy—the juvenile type; or you may have the exact appearances of pseudo-hypertrophic paralysis, coming on in adult life, i.e., as a juvenile form.

'Further, we not infrequently see the different forms passing into one another in the course of their development. A case that began as pseudo-hypertrophy takes afterwards the juvenile or infantile form; a hereditary case turns into a pseudo-hypertrophic or juvenile case, and so on. We frequently come across cases, also, which I should like to call indeterminate or, better, indeterminable forms, cases in which there may be doubt as to which type they belong to. We have seen an example of this in our fourth case, and to a certain extent in the two sisters (cases 5 and 6). In a case of this kind one man sees one type, another, another; or perhaps the case has been taken for a certain type at one time and two years later the physician finds himself inclined or obliged to call it an example af another. And yet all these cases most certainly belong to the same nosological group.

'Different types occur in the same family, and this fact, it appears to me, speaks with great force for the view we are upholding. For in that case they occur in circumstances where there is no room for doubt as to the unity of the disease. For example, the infantile form may appear among children whose father has the juvenile form (observed by Duchenne, Landouzy-Déjerine, Trosier-Guinon and others), or different types may occur in a family in which the hereditary form has already gained a footing. These are, I think, very convincing proofs.

'I believe that the facts I have laid before you in the present state of our knowledge, and disregarding just now the proof from pathological anatomy, to which I shall return later, are sufficient to allow you to recognise in all the different types one nosological species. It is fitting that we should have for this a short distinctive name, and I proposed as such *Dystrophia muscularis progressiva*. I still think that it is the best, and that it involves fewer assumptions than any of those that have been proposed by others.'[1, 2]

Classification and Varieties.—*Before describing the special* features of these different varieties or types in more detail, it may be well to say a word or two with regard to classification.

The more important types or varieties of myopathic atrophy which have been described are as follows:—

1. *Pseudo-hypertrophic paralysis.* In this form, the muscular weakness and atrophy commence in the muscles of the legs or back, and the calf muscles are enlarged from pseudo-hypertrophy.

2. *The 'juvenile form' of progressive muscular atrophy of Erb.* In this form, the atrophy usually commences in the muscles of the shoulder girdle and upper arm, and the deltoids (amongst other muscles) are enlarged.

From the following passage it would appear that Erb intended to include under the term 'the juvenile form of progressive muscular atrophy' all cases of progressive muscular atrophy of myopathic origin. He says:—

'At that time (1883), grounding on numerous cases of my own I made an attempt to show that this apparent unity contained at least two clinically and probably anatomically different forms of disease, and that these were clearly distinguishable throughout in symptoms, development, localisation, and actual condition of the tissues. By the side of the well-defined spinal form, which depends on a lesion of the anterior horns of grey matter, I placed another, which I called 'juvenile' muscular atrophy, and I sought then to

[1] 'The name chosen by Fr. Schultze, "Progressive muscular wasting associated with hypertrophy," is too cumbrous, and scarcely suitable for others than Germans. The "Myopathie atrophique progressive" of Landouzy and Déjerine takes no account of the hypertrophy that is generally present. Charcot's "Myopathie progressive primitive" would suit best of all if it were only certain that the myopathy is primary.'

[2] *Clinical Lectures by German Authors* (Sydenham Society's Translation), page 247.

show in detail that the pseudo-hypertrophic paralysis and the hereditary form of Leyden both belong to the latter type.'[1]

3. *The 'facio-scapulo-humeral type' of progressive muscular atrophy* of Landouzy and Déjerine, which had been previously described by Duchenne as the *infantile form of muscular atrophy*. In this form, the atrophy commences in the muscles of the face and may subsequently involve the muscles of the shoulder girdle, upper arm, back, etc.

4. *The hereditary form of progressive muscular atrophy* of Leyden. In this form the muscular weakness and atrophy commence in the muscles of the back or lower extremities; the calf muscles are often enlarged.

5. *The (purely) atrophic form of myopathic muscular atrophy.*[2] In this form, the muscular weakness and atrophy commence in the back or lower extremities; the cases only differ from Leyden's type in this particular that the calf muscles are not enlarged.

Identity of these different forms.—Almost all authorities are now agreed that Erb's juvenile form and the facio-scapulo-humeral type of Landouzy and Déjerine are mere varieties of the same condition.

The hereditary form of Leyden and the cases which I am in the habit of terming the purely atrophic form are undoubtedly mere varieties of pseudo-hypertrophic paralysis.

Further, it seems to me highly probable, as Erb has suggested, that all of these forms are mere modifications or varieties of the same disease. The differences which seem at first sight to exist between pseudo-hypertrophic paralysis, on the one hand, and the juvenile form of myopathic atrophy and the facio-scapulo-humeral type of Landouzy and Déjerine, on the other, are probably not real points of distinction.

6. *The diffused form of progressive muscular atrophy of infancy and early childhood.*—As I shall afterwards point out, this appears to be a distinct clinical type. It is doubtful whether it is a myopathic or a myelopathic form. Personally, I am disposed to agree with the latter view and to think that the cases which are usually grouped under this head are probably identical with those described by Duchenne under the term *paralysie générale spinale antérieure subaiguë*.

7. *The peroneal type of progressive muscular atrophy.*—This form is undoubtedly distinct from the others enumerated above. Its exact pathology is still undetermined. Some writers have supposed that it is a myopathic, others a neuropathic, and others again a myelopathic, atrophy. As I shall presently point out, in some of its clinical features it seems to bear a close resemblance to the Aran-Duchenne type of progressive muscular atrophy—a fact which, so far as I know, was first insisted upon by Sachs.

The classification, then, of the forms of progressive muscular atrophy enumerated above which, in the present position of our knowledge, seems to me the most satisfactory, is as follows:—

1. *Myopathic atrophies (Progressive muscular dystrophies).*
   Varieties:—(*a*) Pseudo-hypertrophic paralysis.
   (*b*) Juvenile form of progressive muscular atrophy of Erb.
   (*c*) Facio-scapulo-humeral type of Landouzy and Déjerine.
   (*d*) Hereditary form of progressive muscular atrophy of Leyden.
   (*e*) The (purely) atrophic form of progressive myopathic atrophy.
2. *The diffuse form of progressive muscular atrophy of infancy and early childhood.* (Probably myelopathic.)
3. *The peroneal type of progressive muscular atrophy.* (Probably neuropathic or myelopathic.)

[1] *Clinical Lectures by German Authors*, Third Series (Sydenham Society's Translation), page 235.

[2] I refer to the clinical characters. It is probable that in some of the cases in which there is no obvious hypertrophy when the patient comes under the notice of the physician, some muscular enlargement had previously been present; and that in other cases, there is some relative enlargement; the calves, for example, though not actually enlarged, may be relatively large in comparison with the thighs or upper limbs.

PSEUDO-HYPERTROPHIC PARALYSIS

Synonyms.—Atrophia musculorum lipomatosa, Lipomatous myo-atrophy, Pseudo-hypertrophy of muscles.

Pseudo-hypertrophic paralysis is a very interesting and somewhat rare disease.

It is essentially characterised by slowly developing muscular weakness and muscular atrophy, and by the enlargement of some of the muscles which are undergoing the atrophic process. The increased size of the muscles is not a true hypertrophy, but is due to the production in the muscles of an excess of fat and fibrous tissue. Hence the term *pseudo-hypertrophic* paralysis.[1]

Morbid Anatomy.—In its slow development, progressive course and the marked muscular weakness and muscular atrophy by which it is characterised, pseudo-hypertrophic paralysis resembles the Aran-Duchenne type of progressive muscular atrophy; and, as I have already remarked, it was at one time supposed that, like the spinal form of progressive muscular atrophy, the disease was due to a lesion of the anterior cornual region of the spinal cord. I need not again discuss this question in detail. Suffice it to say that it is now generally believed that the muscular wasting is myopathic; that is to say, that it is due to an affection of the muscular tissue itself, and that it is not the result of a lesion of the spinal cord or peripheral nerves.

Pseudo-hypertrophic paralysis, though not a very rare, is by no means a very common disease; and the opportunities for investigating the pathology after death seldom occur. The number of cases which have been examined after death is surprisingly small—out of proportion small to the frequency with which the disease occurs. In proof of the statement, that the disease is not very rare, I may mention that at the present time I have eleven cases under observation—two in Edinburgh and nine in other parts of the country. The paucity of

[1] Recent observations would seem to show that this statement cannot be absolutely applied to all cases. Erb, for example, states with regard to one of his cases:—'According to former usage this case also would have been termed pseudo-hypertrophic paralysis without much ado, although as you have satisfied yourselves, the muscles that are enlarged and are acting well by no means give the impression of pseudo-hypertrophy or lipomatosis.'

autopsies is no doubt explained by the facts that the patients very rarely die in hospital, and that post-mortems involving the examination of the spinal cord are seldom made in private practice.

In the great majority of the (undoubted) cases of pseudo-hypertrophic paralysis which have been examined after death, the spinal cord was perfectly normal; and in the comparatively few cases in which the peripheral nerves seem to have been carefully examined, there was no lesion in this part of the nervous apparatus.[1]

In the few cases of pseudo-hypertrophic paralysis in which pathological changes were present in the spinal cord, the alterations were probably associated or accidental lesions.

In one case which I examined some years ago, the grey matter was curiously malformed in the cervical region (see Plate LXXXVI. fig. 1).

In another case which has recently proved fatal, the spinal cord is also misshaped. (See Plate LXXXVI. figs. 2 and 3.) A fissure dips down into the posterior horn of grey matter on the left side of the lumbar enlargement. I first became aware of the presence of this fissure when I came to cut up the partially hardened cord into suitable pieces for microscopic examination. Not suspecting any naked eye lesion, I had not carefully examined the exterior of the cord in the fresh state. The fissure was quite apparent to the naked eye. The intermediate grey matter is disintegrated and the distribution of the nerve cells in the posterior part of the cord (posterior column and posterior part of the lateral column) is, so far as my experience enables me to judge, peculiar. Two sections of the cord which Dr. Muir has kindly prepared for me are represented in Plate LXXXVI. figs. 2 and 3. I feel great hesitation in expressing a positive opinion as to the significance of the changes which are present in these sections. They can only be the result either (*a*) of artificial damage to the cord, say by the point of the bone pliers in removing it from the body; (*b*) of congenital malformation; or (*c*) of disease. The fissure in the cord (whether originally due to artificial damage or to disease) may no doubt have been exaggerated and enlarged by the process of hardening.

That some of the changes are artificial I have little doubt, but that they are altogether due to this cause is by no means clear. I fail to see, for example, how the condition represented in fig. 3, Plate LXXXVI., could be altogether the result of artifical damage. Dr. Muir takes a different view. After very careful examination, he concludes that there is no structural alteration which must necessarily be looked upon as ante mortem.[2]

Professor Sherrington, who has also kindly examined the sections, admits the great difficulty there is in forming an opinion as to the significance of the alterations, and states:—'I do not think the cavity in your preparation explicable as an ante-fact.[1]

Further, somewhat similar alterations have been described by independent observers.

In a case reported by Drummond, the grey matter of the anterior horn, at its junction with the posterior cornu and in its lateral part (*the same situation affected in my cases*), was softened and disintegrated, so that a cavity was formed in the centre of the cord; this cavity, which had no proper cyst wall, was of large size in the lumbar enlargement, where it caused the cord to bulge out laterally, and extended through the dorsal and cervical regions; 'with a high power, minute disintegration could be traced through the lateral grey net-work of both sides, the degenerative appearances being most conspicuous around the blood-vessel.'

In another case (which was examined by Gowers and Lockhart Clarke) 'at the lower dorsal segment, there was an area of granular disintegration in the intermediate grey substance on each side, in front of the posterior vesicular tract' (*the same portion of the grey matter which was affected in my two cases and and in Drummond's case*). 'This part was unduly translucent for half a centimetre in vertical extent, and in the middle of this area the disintegration had produced an actual cavity, across which the fibres for the cerebellar tract ran unchanged.'[2]

It is possible that the changes in the intermediate grey matter which were present in all of these cases were the result and not the cause of the disease. But in my first case, the malformation of the grey matter was clearly congenital. I do not, of course, suggest that this malformation was the cause of the lesions in the muscles; but I am strongly inclined to think that it was not merely accidental. It suggests that in pseudo-hypertrophic paralysis there is a widespread tendency to congenital or developmental defects in the neuro-motor apparatus

[1] On this point see page 204.

[2] In the report which Dr. Muir has kindly furnished me with, he says:—'What is the nature of the fissure? In favour of part at least being natural is the regularity of the margins and the condensation, and so much is this the case at places that it is difficult to conceive of its being produced by artificial means. But, on the other hand, so far as I can find after careful examination of the edges, there is no structural alteration which must necessarily be looked upon as ante mortem. The surface of the cord also shows signs of injury posteriorly, in the stripping of the pia, displacement of the nerve roots, etc. My impression at first was that there had probably been an elongated area of softening in the posterior cornu which had been artificially extended to the surface, but this supposition would not explain the position of the left posterior column at the higher level described, *i.e.* before the fissure reaches the surface. At this level the left posterior column is much smaller than the right. It must either have been so naturally—which is not the case at higher and lower levels in the cord—or a portion must have been shaved off when the pia was removed. So far as I can see, it is impossible to come to an absolute conclusion, but I do not think there is sufficient evidence from the sections alone to enable one to describe the changes as being undoubtedly ante mortem.'

[1] Professor Sherrington's full report is as follows —

'The specimen was certainly well hardened, an important point in judging of the character of the fissure and cavity. I think some of these fissures offer the hardest problems in morbid histology.

'The appearance of a condensed edge can be sometimes given and closely resemble a sclerosed edge even in a purely artificial cavity. Some years back I made a number of artificial cavities in portions of spinal cord purposely by bending the pieces of cord at a not very sharp angle and tying them in that position and then hardening in Muller's fluid. The cavities obtained nearly always affected the posterior column and always ran into the grey matter opening there into a larger space. The sections through such ante-facts do not, however, agree in character with the appearance in your specimen. I do not think the cavity in your preparation explicable as an ante-fact.

'By hardening in bichromate we sacrifice the grey matter—except the borders of the coarser ganglion cells in it—for the sake of the white column. The spongiosa is shrunken much more than the white matter, as can be seen by its sunken level at the ends of a block of cord hardened in Muller. Also the connective tissue shrinks (even the tough dura) much more than the white matter. If a short length of cord with dura slashed tranversely over one half and left without transverse cuts over the other half, be placed in bichromate, an hour's time is enough to curve it strongly over toward the side of the unslashed dura.

'Cavities which are ante-facts are, I am convinced from what I saw at that time, due to unequal shrinkage of grey matter and connective tissue on the one hand and of white matter on the other, resulting in rending and cleavage. The cavity in your preparation gives me, on detailed examination, the impression that it has extended to the surface in the hardening. I am led to think there was no fissure which reached the cord in the fresh state, but that in the depth of the posterior horn, or posterior part of grey matter further forward, there was either an actual cavity or a region of altered, loosened, atrophic tissue which, under hardening and dehydration, shrank greatly, splitting, as it did so the weakest part of the wall of tissue adjoining. I imagine this happened when in the bichromate and before the preparation was placed in spirit, because the tissue bounding the cavity and cleft bear marks of having been particularly under the action of bichromate.'

[2] Gowers' *Diseases of the Spinal Cord*, Second Edition, p. 516.

—not merely in the muscles but in the spinal cord and perhaps (as Von Babes' observations to which I have already referred would seem to show) in the nerve-terminations in the muscles.

In my first case, large collections of leucocytes of a rusty red colour were scattered here and there through the grey matter, more especially in the cervical region; the nervous elements around some of these extravasations seemed to be in a condition of inflammatory irritation, some of the axis-cylinder processes being hypertrophied; the nerve cells were very numerous, some of them appeared to be enlarged. These changes (exudation of leucocytes, etc.) were probably accidental or associated lesions. It is very improbable, I think, that they were in any way connected with the changes in the muscles. It must be remembered that in the great majority of cases of pseudo-hypertrophic paralysis which come under the notice of the pathologist, the disease is of long standing; indeed in most cases, the patient has, for several years before death, been a helpless cripple. Under such circumstances, it is not unreasonable to suppose that pathological alterations, totally unconnected with the causation of the disease, may occasionally be developed in the spinal cord before death.

Great caution is therefore required in drawing conclusions as to the significance of any alterations in the spinal cord which happen to be present.

In my second case (represented in Plate LXXXVI. figs. 3 and 4) the multipolar nerve cells in the anterior horn were numerous and large, many of them were slightly fatty and their nuclei somewhat less distinct than normal.

So far as I know, there are no facts either clinical or pathological (except Von Babes' observations) to support the view that the morbid process in the muscles has its starting point in the peripheral nerves. Von Babes' observations, if confirmed, would seem to show that the end-plates and fine terminations of the motor nerves in the muscles are imperfectly developed or degenerated. The facts that in cases of pseudo-hypertrophic paralysis the muscular co-ordination is so remarkably perfect and that there is very rarely, if ever, any trace of the 'reaction of degeneration' in the affected muscles are difficult to reconcile with this (Von Babes') view.

The very remarkable way in which patients affected with pseudo-hypertrophic paralysis can co-ordinate their movements and balance themselves in the erect position, even when their muscular power is very greatly enfeebled, seems conclusively to show that there is no interference with the muscular sense and with the ingoing impressions concerned in muscular co-ordination, which pass from the muscles to the spinal cord. We may confidently, I think, conclude that the sensory nerves of the muscles are entirely unaffected.

Further, as I shall afterwards point out, the sensory functions of the skin are absolutely uninterfered with. The defect, whatever it may be, is clearly confined to the motor or trophic-motor side of the nerve apparatus or to the muscles themselves.

The histological changes in the muscles.—The most striking pathological changes in the muscles after death are (1) an overgrowth of the fatty and interstitial fibrous tissues, and (2) an atrophy of the muscular fibres themselves. In advanced cases, the muscular tissue may, on naked eye examination, seem to have completely disappeared and the muscles may look like masses of fat.

On microscopic examination, the muscular fibres and bundles of muscular fibres are seen to be separated by large masses of fat cells and an excessive quantity of interstitial connective tissue. (See Plate LXXXVI. figs. 4 and 5.)

In the advanced stages of the disease, many of the muscular fibres are markedly atrophied. The atrophy seems in part to be a simple atrophy, in part a degenerative process. Many of the most minute (atrophied) fibres still retain their transverse striation, while others are degenerated, vacuolated, split up longitudinally or in process of transformation into fibrous tissue.

Some of the muscular fibres are enlarged, but this change (hypertrophy of the individual muscular fibres) is much less conspicuous in pseudo-hypertrophic paralysis than in some of the other forms of progressive muscular dystrophy. The connective tissue and blood vessels between the atrophied fibres are usually very rich in nuclei. So far as my observation enables me to judge, this change is especially marked in the earlier stages of the disease. In the later stages, the interstitial tissue between the wasted fibres consists chiefly of fat cells.

As I have already remarked, some authorities suppose that the atrophy of the muscular fibres is secondary to the interstitial changes; and, so far as I can judge, this is partly true, but I doubt if it expresses the whole truth. The weight of clinical and pathological evidence seems to me to be in favour of the identity of this (the pseudo-hypertrophic) and the other forms of myopathic atrophy; and it must I think be acknowledged that in the non-pseudo-hypertrophic forms of myopathic atrophy the wasting of the muscles is chiefly due to a degenerative process, and is not merely the result of a simple atrophy from pressure.

In connection with this point it must be remembered that too much importance should not be attached to the examination of the muscles in old-standing cases of pseudo-hypertrophic paralysis. In many of the cases which have been examined, the disease has been in existence for many years and at the time of death the final stage of atrophy has been reached. For the purpose of demonstrating the mode of development of the muscular changes, the condition of the muscles in the early stages of the disease is far more important than the condition in the last stages of the atrophy.

In this, as in other forms of myopathic atrophy, the enlargement (apparent hypertrophy) of certain muscles (the calf muscles and the spinati muscles, for example) is associated with atrophy of other muscles. This combination of atrophy and apparent or pseudo-hypertrophy is a characteristic of the disease. So far as one can judge from the condition of the muscles during life, the atrophy in some of the muscles is a simple atrophy. In many of the muscles, it is not, so far as one can see with the naked eye, preceded by any enlargement. But after death, the muscles which have apparently undergone this simple atrophy are in many cases infiltrated with fat and similar, so far as their histological characters are concerned, to the muscles which were formerly enlarged.

These pathological changes are not entirely confined to the voluntary muscles; for in one of my cases the muscular tissue of the heart was affected. (See Plate LXXXVI. fig. 6.)

In the advanced stages of old-standing cases (see Plate LXXXVIII. figs. 1 and 2) the subcutaneous fat may entirely disappear just as it does in the advanced stages of progressive muscular atrophy. But the development of the bones, in length at all events, does not seem to be interfered with. This is a point of some interest.

Etiology.—Pseudo-hypertrophic paralysis is essentially a

disease of childhood, and is much more common in boys than in girls. The disease usually commences before the sixth or seventh year. In some cases, the symptoms are first noticed when the child begins to walk; in others, the onset does not occur till later childhood; in rare cases, the symptoms are first noticed at or about the time of puberty. In the, comparatively speaking, rare cases in which the disease appears to commence after the development of the body has been completed (at or after the age of 20) it is usually mild in type and has in all probability been slowly and insidiously progressing for some time before it was sufficiently marked to attract the attention of the patient. In girls, the disease is usually developed later than in boys; and in girls, the disease is usually less severe than in boys. In fact, speaking generally, we may say that the earlier the disease is developed, the more severe is its type and the more rapid its progress; and *vice versâ*, the later it is developed, the less severe is its type and the less rapid its progress. There are, of course, exceptions to all of these statements.

Further, it seems probable that the later the disease is developed the more likely it is to assume the form which has been described by Erb as the juvenile type of the disease.

The disease usually begins insidiously, without any apparent cause. In rare cases, the onset is preceded, or appears to be preceded, by an attack of measles, scarlet fever, or some other infantile complaint; but in many of the cases in which measles or other acute diseases appear to the parents to be the cause, the disease was in all probability already present and unrecognised. At the time of birth and during early childhood (i.e. up to the onset of the disease), the patients present no peculiarity; they are usually quite healthy up to the time at which the disease develops; but in other cases they are longer in walking than most healthy children.

Pseudo-hypertrophic paralysis is essentially a 'family disease'; it is quite common to find several members of a family, usually several brothers, less frequently the sisters as well as the brothers, affected. The disease is clearly due to something which is born with the individual—to something which is handed down from the parent to the children. The disease is rarely directly hereditary (i.e. the parents of children who manifest the disease are very rarely themselves affected); but the uncles, aunts, grand-uncles or grand-aunts, and (far more frequently) the male cousins may have been affected. In several of my own cases, the hereditary tendency could not be traced, and in at least three instances one member of a family only was affected. It is of course possible, indeed probable, that in some of these cases other members may ultimately become affected.

When successive cases occur in different generations, the disease is almost always passed on through the female line. Exactly the same thing is seen in Friedreich's ataxia. It necessarily happens that pseudo-hypertrophic paralysis can rarely be directly handed on from parent to child; for the males who are affected with the disease are usually helpless cripples by the time of puberty, and females who are affected are not likely to be chosen in marriage, although in them the disease is often only slight when they attain the marriageable age. But this statement only affords a partial explanation of the fact that the disease is almost exclusively handed down through the female line; for the male children of the healthy brothers of pseudo-hypertrophic patients usually escape, while the male children of the healthy sisters are often affected.

It is doubtful whether a neuropathic inheritance has much to do with the production of the disease.

Some writers state that the disease is as common in the upper as in the lower ranks of society, but this is not my experience; with very few exceptions my cases have occurred in hospital patients.

Clinical History.—The essential clinical feature of pseudo-hypertrophic paralysis is a slowly-developing and gradually-increasing muscular weakness, with enlargement of some and atrophy of other muscles.

As I have already pointed out, the disease usually begins in childhood, in the great majority of cases before the seventh year. In some cases, the muscular defect (weakness) is noticed from the time that the child begins to walk. The first symptom to attract attention is usually clumsiness and insecurity in the gait; the child stumbles or falls without sufficient cause. In some cases the parents are astonished that the child is so weak on its legs; for, as they will sometimes tell you with pride, 'its calves are finely developed.' As the disease progresses, the gait becomes waddling in character

Duchenne divided the disease into three stages:—The *first* characterised by difficulty in standing and walking, and weakness of the muscles of the lower extremities and of the sacro-lumbar region; the *second* by muscular hypertrophy; and the *third* by increasing feebleness of the muscles both of the upper and lower extremities. But these stages are only roughly speaking and approximately accurate; for modern observations have abundantly shown that at the same time that some of the muscles are enlarged (apparently hypertrophied) others are atrophied. It is important to note that many of the muscles which are atrophied never present any previous stage of enlargement or pseudo-hypertrophy.

The first symptom is usually weakness in the muscles of the back and legs. As the disease progresses and the weakness becomes more marked, the back becomes curved, the attitude and gait become characteristic, and the child has difficulty in rising from the recumbent to the erect position.

The attitude.—In well-marked cases (i.e. when the disease is typical and fully developed), the patient usually stands with his feet wide apart (see Plate LXXXVII. figs. 1 and 2) so as

Fig. 7.—*An advanced stage of pseudo-hypertrophic paralysis, showing the position of the feet in the erect position of the body.*

to enlarge his base of support as much as possible; the heels are in many cases drawn up in consequence of retraction of the calf muscles (see fig. 7); the back is strongly curved in the lower dorsal and lumbar regions (lumbar lordosis), the

shoulders are drawn far back and the abdomen is prominent; in some cases (as Duchenne has pointed out) a line drawn vertically downwards from the middle of the shoulders falls behind the sacrum (see fig. 8). In many cases the chest is flattened in the antero-posterior direction.

When the patient stands erect or when he attempts to walk, the arms are usually extended by the sides and used to balance the body. The attitude is a very striking one, and it is remarkable how, even in the comparatively speaking advanced stages of the disease when the muscular debility is extremely great, the patient is able to maintain his balance in the upright position. As I have already remarked, there is no defect of co-ordination; in fact, the patient's power of balancing the body and adjusting his equilibrium under the very unfavourable circumstances in which he is placed in consequence of the muscular weakness is a remarkable feature of the disease. But although the patient can stand and maintain his equilibrium so long as he is undisturbed, he is extremely insecure; the slightest push in any direction is sufficient to throw him over; a mere breath of wind is almost sufficient to knock him down; and if his centre of gravity is displaced he falls down with a thump—all of a heap as it were.

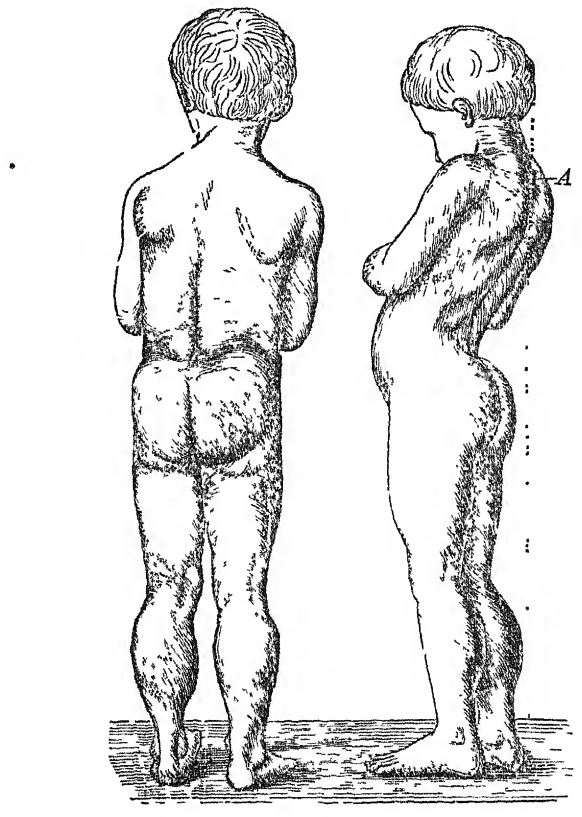


Fig. 8.—*Pseudo-hypertrophic paralysis, showing enlargement of the calves and buttocks. The back is curved, and a line drawn downwards from the scapula falls behind the sacrum.—(After Duchenne.)*

The antero-posterior curvature, which is such a striking feature when the patient stands erect, entirely disappears when he assumes the sitting position. Duchenne believed that this curvature was due to weakness of the spinal muscles; but some authorities think that it is rather the result of weakness of the extensor muscles of the hip.

The gait.—In most cases the gait is, even in a comparatively early stage of the disease, very characteristic. The body oscillates or sways from side to side; the gait is waddling in character and in some cases high-stepping. There is great difficulty in flexing the thigh on the abdomen, in projecting the thigh forwards and in raising the toes from the ground; consequently even at a comparatively early stage of the disease (i.e. when the patient can walk on the flat) he is unable to go upstairs. He has to drag himself up by the handrail. In many cases even in the early stages of the disease, the patient cannot raise himself on his toes and cannot jump. In the great majority of cases of pseudo-hypertrophic paralysis it will be found on inquiry that the patient has never been able to move (run and jump) as freely and actively as a healthy child does.

In some cases in which the motor defect is more marked, although the foot is raised from the ground the patient is unable to advance it; and instead of progressing forwards he may go slightly backwards at each step, owing to the foot, after being raised from the ground, falling back further than it was before. Patients affected with pseudo-hypertrophic paralysis are usually unable to seat themselves slowly and steadily down on a chair; they go down suddenly, all of a heap.

The attitude and gait which I have just described may be absent or very slightly marked in those cases in which the hypertrophy of the calf muscles is absent or slight. I had recently under my care in hospital a very interesting and important case of this kind, the details of which are mentioned below (see page 91).

Peculiar method of rising from the recumbent position; climbing up the thighs.—Another remarkable peculiarity which results from the muscular weakness is a great difficulty which the patient experiences in rising from the recumbent and sitting postures. Indeed, in advanced cases he may not be able to raise himself at all. Even in the earlier stages of the disease, he makes use of his arms, catching hold of chairs or other pieces of furniture and drawing up his body by the aid of the upper extremities

When he is laid flat on his back on the ground and made to rise, without having anything to take hold of, he usually goes through a series of movements which are represented in figs 9, 10, and 11. In many cases, he first turns on his face; he then gets with great difficulty on to his hands, the head hanging down between the arms. From this position, he gradually extends himself, first raising one leg and then the other, and finally 'climbs up his thighs,' as it has been termed. The hip joint is extended by grasping the thigh with the hand and the body is pushed up, as it were, by the arm.

In some cases, the feet are placed close together before the patient raises himself to the erect position. In one of my cases, after the patient had raised himself on to his toes and fingers, the foot and leg were drawn forward by means of the hand (see Plate LXXXIX. figs. 1 and 2). In another, the legs were always placed extraordinarily wide apart (see fig 11). It was a remarkable proof of the patient's co-ordinating power that he was able to raise himself with a jerk from this into the erect position. When this patient came under my notice there was little or no muscular enlargement (see Plate LXXXVIII. figs. 4 and 5) and the case might easily have been placed under the atrophic form; but the calves, which were still relatively large, had at a previous stage of the case been very much enlarged.

The peculiar manner in which the patient rises from the ground and climbs up his thighs is very characteristic, though not pathognomonic. It may occur in any condition in which there is great weakness of the extensor muscles of the hip. I have seen it in children affected with rickets and in an adult woman who suffered from a diseased (malacostial) pelvis.

Even at an early stage of the disease, the patient experiences difficulty in going upstairs. This and the high action gait are

due to the fact that the muscles which flex the thigh on the abdomen are generally affected in an early stage of the case.

Should the patient come under observation at an early period of the disease, the calf muscles will probably be found to be large, firm and elastic; in many cases they feel like hard masses of india-rubber. The enlarged muscles stand out prominently, as if they were in a permanent condition of contraction; but notwithstanding this apparent hypertrophy their motor power is (usually) markedly impaired The amount of contraction, too, which can be produced in them by a powerful faradic current is below the normal.

In some cases, the gluteal muscles or the muscles on the front of the thigh are also enlarged. The deltoids and infraspinati are in many cases markedly enlarged—apparently hypertrophied. The enlargement of the infraspinati was very remarkable in the case which is represented in Plate LXXXVII. figs. 1 and 2.

In rare cases (see fig. 12), almost all the voluntary muscles of the body may become enlarged. This, however, is quite exceptional.

In the great majority of cases, muscular atrophy is a prominent feature even in the earlier stages of the disease. The latissimus dorsi and the lower portion of the pectoralis major are almost invariably wasted. As Gowers has pointed out, this is a point of great diagnostic importance.

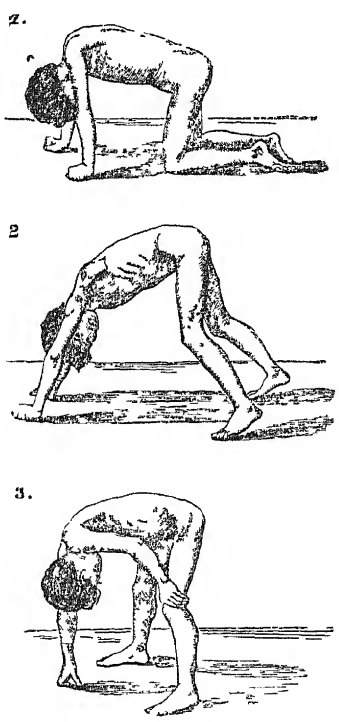


Fig 9 —*The attitudes which patients with pseudo hypertrophic paralysis assume in rising from the recumbent to the erect position —(After Gowers.)*

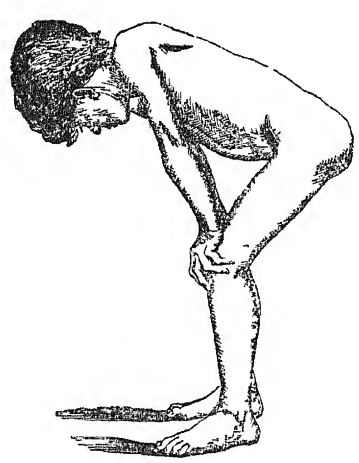


Fig. 10.—*Climbing up the thighs in pseudo-hypertrophic paralysis — (After Gowers)*

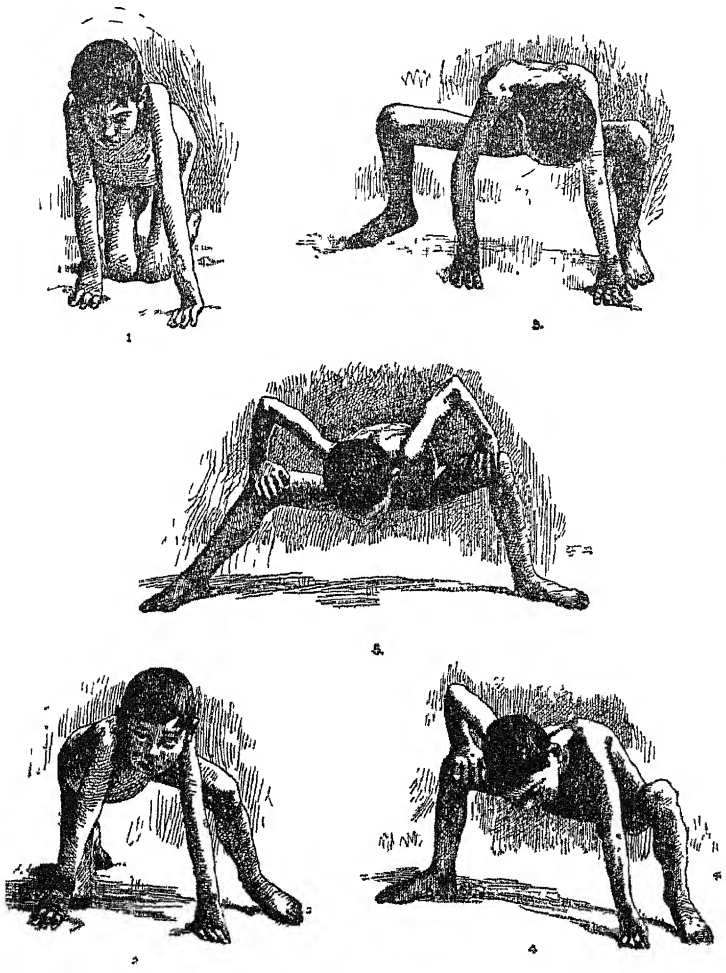


Fig. 11 —*Method of rising from the recumbent to the erect position in the case of pseudo-hypertrophic paralysis represented in Plate LXXXVIII. figs. 4 and 5.*

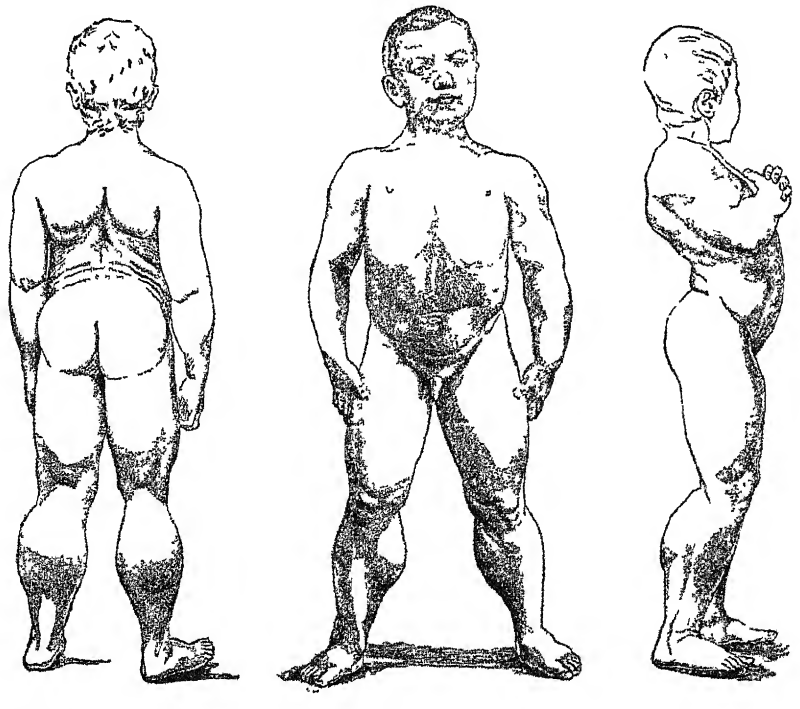


Fig. 12.—*A case of pseudo-hypertrophic paralysis, in which almost all the muscles of the body were hypertrophied.—(After Duchenne.)*

The small muscles of the hand (fingers and thumb) are very rarely affected in the early stages of the disease; but they may be atrophied in the terminal stages. The muscles of the face and neck are very rarely indeed affected in a marked degree, and it is only in exceptional cases that the tongue is involved.

In the later stages, the hypertrophied muscles become atrophied; and in the course of time, provided the patient lives long enough, almost all the voluntary muscles of the body (the intrinsic muscles of the hand and the muscles of the face and neck usually excepted) may appear to have completely disappeared.

The case which is represented in Plate LXXXVIII. figs. 1 and 2 shows the last stage of the disease. The history of the case is detailed below.

In the advanced stages of the disease, the spinal column is often markedly curved (see Plate LXXXVIII. figs. 1 and 2).

When the latissimus dorsi and pectoralis muscles are weak and atrophied, the shoulders offer no resistance but are pushed up towards the ears when an attempt is made to raise the patient into the air, the hands being placed under the armpits (see Plate LXXXVII. fig. 3). Erb lays stress upon this and also upon the fact that if the arm, raised to the horizontal level, is brought forcibly down against powerful opposition, the scapula is drawn strongly towards the upper arm and its angle is moved outwards, in consequence of defective fixation by the trapezius and rhomboids. The inability to fix the scapula to the thorax is well seen in Plate LXXXIX. fig 3.

The condition of the muscles.—As I have already stated, some of the muscles appear to be hypertrophied, while others are atrophied. As the disease advances, the enlarged muscles waste. Fibrillary twitchings are very rarely indeed present. Erb says very emphatically that fibrillary tremors or twitchings are never present. With this opinion I am unable to agree. In the case which is represented in Plate LXXXVII. figs 3 and 4, fibrillary twitchings were very conspicuous in the muscles of the back, which were very markedly atrophied, they were also occasionally noticed in some of the muscles of the limbs. The case is of great interest not only because of the presence of fibrillary twitchings but because it conclusively shows the identity of pseudo-hypertrophic paralysis with the atrophic form of progressive muscular atrophy.

The case is afterwards described in detail.

In cases of pseudo-hypertrophic paralysis, the wasted muscles respond feebly to electric currents (simple diminution), but the reaction of degeneration is rarely, if ever, developed. The faradic irritability diminishes as the muscular atrophy increases; in the later stages the atrophied muscles may fail to respond to either form of current.

The mechanical irritability is also diminished.

In the advanced stages of the disease, contractures at the ankle, knee and elbow, less frequently at the hip, are often produced (see Plate LXXXVIII. figs 1 and 2).

The condition of the reflexes.—In the earlier stages of the disease, the reflexes may be unaltered; but in those cases in which the muscles on the front of the thigh are markedly affected, the knee-jerks may be absent at a comparatively early period of the case. The skin reflexes are usually preserved for a long time.

The functions of the bladder and rectum are seldom interfered with, but occasionally a temporary condition of incontinence occurs in the later stages of the disease.

Provided that the patient attains the age of puberty, the sexual development takes place in the normal manner. In some cases it is precocious.

Vasomotor and trophic alterations.—The nutrition of the bones does not seem to be interfered with. The osseous development goes on. In the case which is represented in Plate LXXXVIII. figs. 1 and 2, the bones seemed to have developed, as regards their length at least, quite normally.

The skin of the legs and thighs often has a mottled appearance; this is not constant and is by no means pathognomonic. I have noticed exactly the same appearance in several other conditions, notably in the spastic paraplegia of early life. In some cases, the feet and hands are blue and cold. The surface temperature is in some cases subnormal.

Sensory functions.—The sensory functions of the skin and the special senses are always quite normal.

Mental condition.—The intellectual faculties and cerebral functions are, in many cases, absolutely normal. Some of the patients affected with pseudo-hypertrophic paralysis are intellectually above the average. The patient represented in Plate LXXXVIII. fig 1, was mentally very acute; he employed his time in reading all sorts of literature. In other cases, the mental faculties are imperfectly developed; occasionally the patient is quite idiotic. The patient who is represented in Plate LXXXVII. fig. 6, is intellectually very much below the average; his brother, who is also affected, is mentally very deficient; and his sister, who presents none of the features of the disease, is deranged and in an asylum

Course and Duration.—The duration of pseudo-hypertrophic paralysis varies very considerably in different cases. The disease generally runs a very chronic course. Cases which develop soon after birth seem, as a rule, to progress more rapidly than those which are developed about the age of puberty. This fact is perhaps due to the circumstance that the tendency to the disease is born with the individual, and that the stronger the congenital tendency, the earlier is the disease likely to manifest itself and the more severe is it likely to be. Girls, as I have previously remarked, are usually attacked later than boys; and in girls the disease is usually less severe than in boys.

When the disease does not develop until the period of puberty, the prognosis, as regards duration, is much more favourable.

Death is usually due to the occurrence of some pulmonary complication (such as bronchitis or pneumonia) or other intercurrent disease. A comparatively trivial illness may easily kill when the patient is reduced to the condition represented in Plate LXXXVIII. fig. 1; he died from influenza and bronchitis.

Diagnosis.—In typical cases the clinical picture is so striking that the diagnosis is self-evident, provided of course that the observer has seen a case of pseudo-hypertrophic paralysis before. The attitude and gait, and the peculiar way in which the patient raises himself from the ground by climbing up his thighs (though this is not absolutely pathognomic) are highly characteristic. The enlargement of the calf muscles is, however, the most striking and important feature of this variety of myopathic muscular atrophy from a diagnostic point of view, for in some of the other forms the same attitude, gait, and mode of rising from the recumbent position may be

present. The enlargement of the infraspinati muscles is also of great diagnostic significance. The absence of fibrillary twitchings and the reaction of degeneration are, as I have more than once stated, characteristic features of this and the other forms of myopathic muscular atrophy. The age and sex of the patient are of diagnostic value; and the fact that several members, usually males, in the same family are often affected is very significant. Gowers lays much stress upon the atrophy of the lower part of the latissimus dorsi and pectoralis major muscles.

It is important to remember that the muscular atrophy is in some cases associated with very little or no pseudo-hypertrophy. Unless the observer is well acquainted with the various forms of myopathic muscular atrophy, the true nature of cases of this kind may be easily overlooked, especially if the case is isolated, i.e. when no other members of the family are affected.

To sum up, the most important clinical features of pseudo-hypertrophic paralysis from a diagnostic point of view are :— The slow and gradual onset; the affection of several members, usually boys, in the same family; the gradual and progressive muscular weakness; the enlargement of certain muscles, especially the calf muscles, glutei, infraspinati and deltoids; the atrophy of other muscles, especially the lower part of the latissimus dorsi and pectoralis major; the absence of fibrillary twitchings and of the reaction of degeneration; the peculiar attitude and gait, and the characteristic mode of rising from the recumbent to the erect position; the inability to fix the scapulæ to the thorax; the normal, diminished, or abolished (never exaggerated) condition of the knee-jerks; the normal condition of the bladder and rectal reflexes; and the entire absence of sensory symptoms and of visceral lesions.

The differential diagnosis of pseudo-hypertrophic paralysis and of Friedreich's ataxia.—These diseases have certain features in common. Both are diseases of development (i.e. they very rarely commence after the development of the body is completed); both are 'family diseases' (i.e. they are apt to affect several members of the same family); both produce difficulty in walking; in both, there is muscular weakness; in both, the knee-jerks may be abolished (almost always in Friedreich's ataxia, often in pseudo-hypertrophic paralysis); in both, the spine becomes curved in the later stages; in both, the feet may become distorted (clubbed); and in both, the patient is finally reduced to the condition of a helpless cripple.

But, notwithstanding these points of resemblance, there is no difficulty in distinguishing the two conditions in the earlier stages of the case. In Friedreich's ataxia, the difficulty in walking is due to inco-ordination rather than to pure muscular debility. In pseudo-hypertrophic paralysis, on the other hand, the difficulty in walking is entirely the result of muscular weakness, the co-ordinating power being retained in a very remarkable way. The attitude and gait are quite different in the two diseases. In Friedreich's ataxia, the hands are affected as well as the lower extremities; speech, too, is often involved; whereas, in pseudo-hypertrophic paralysis, the movements of the hands are rarely interfered with even in the later stages, and speech is never affected. The enlargement (apparent hypertrophy) of the muscles which is so characteristic of pseudo-hypertrophic paralysis is never seen in Friedreich's ataxia.. The atrophy of the lower part of the latissimus dorsi and pectoralis major, and it may be of other muscles, is also an important point of difference.

The differential diagnosis of pseudo-hypertrophic paralysis and the spastic paraplegia of early life presents no difficulty. The chief points of distinction are :—

The mode of onset. Slow and gradual in pseudo-hypertrophic paralysis; often rapid as the result of a distinct cerebral lesion, associated with convulsions, or due to an injury received at the time of birth (instrumental delivery) in the spastic paraplegia of infancy.

The condition of the deep reflexes. Normal, diminished or abolished in pseudo-hypertrophic paralysis, exaggerated in the spastic paraplegia of early life.

The condition of the upper extremities. In the former, some of the muscles of the shoulder girdle (especially the lower part of the pectoralis major and the latissimus dorsi) are usually atrophied and others (especially the deltoid and infraspinati) are hypertrophied; while, in the latter, all of the muscles of the upper extremity may be more or less atrophied and undeveloped, or rigid with exaggeration of the deep reflexes.

The attitude and gait. The lordosis, waddling, high-action gait, and peculiar mode of rising from the recumbent to the erect position which are such characteristic features of pseudo-hypertrophic paralysis, are all absent in the spastic paraplegia of early life. In the latter condition, the legs are more or less rigid; when the patient stands or is held in the erect position, the feet tend to cross and to assume the position shown in fig. 13.

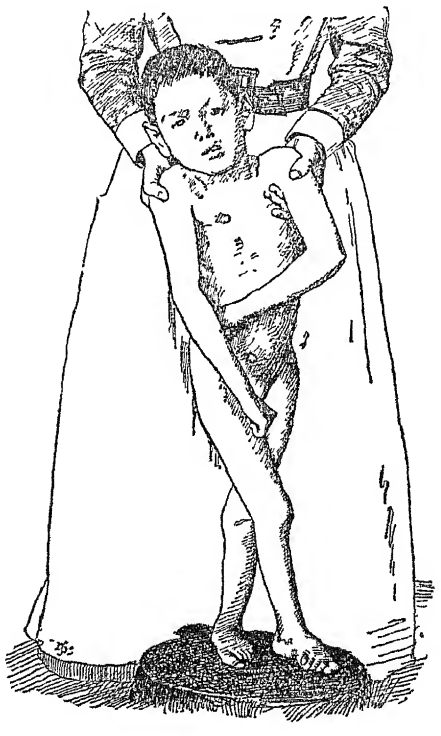


Fig. 13.—*Case of infantile spastic paraplegia (bilateral hemiplegia) dating from the time of birth; showing the attitude and position of the limbs when the patient was supported in the erect position.*

The presence of cerebral symptoms. Although in some cases of pseudo-hypertrophic paralysis the intellectual development is interfered with, this is exceptional; many of the patients are mentally very acute. But in patients affected with spastic paraplegia dating from early life, there is usually some mental impairment, and recurring epileptiform attacks are often present.

The hereditary and family tendency. In cases of spastic paraplegia of early life, the hereditary and family tendency,

which is such a conspicuous feature of most cases of pseudo-hypertrophic paralysis, is entirely absent.

Prognosis.—The prognosis of pseudo-hypertrophic paralysis is very unfavourable. The tendency of the disease is to progress steadily from bad to worse; almost all cases terminate, sooner or later, in death; but in many cases the fatal issue is not reached for several years. When the extreme condition of emaciation which is represented in Plate LXXXVIII. figs. 1 and 2 is reached, the patient may still live for several years, but his tenure of life is very insecure. A slight bronchial attack, or any intercurrent respiratory or other complication may in such circumstances speedily prove fatal. Speaking generally, the earlier the disease is developed, the more rapid is its course; and since the disease usually develops earlier in males than in females, the prognosis as regards the rapidity is worse in boys than in girls.

Treatment.—The treatment which has hitherto been employed has been of little avail We know of no remedy which exerts any distinctly beneficial influence upon the course of the disease. The general health must be kept in the best possible state of efficiency. The patient should be well-fed, well-clothed and have plenty of fresh air. General tonics, more especially cod-liver oil, are advisable. The nutritive condition of the affected muscles should be, so far as possible, maintained by judicious massage, suitable gymnastics, systematic muscular exercises and the faradic current. Duchenne states that he cured two cases of the disease by the interrupted current; and Erb thinks that electrical treatment is the most important means of influencing the disease which we possess. He advises that the galvanic current should be applied to the spine over the lumbar and cervical enlargements of the cord, with the object of acting upon the trophic centres situated in these regions; and that the faradic, galvanic, or faradо-galvanic currents should be applied directly to the muscles and nerves. Strong currents and long applications must not, however, be employed.

Gowers has pointed out that when, from any cause, the patient ceases to walk, the weakness in the muscles is apt to increase rapidly. Contractures and deformities which interfere with walking should therefore, if possible, be prevented by passive exercise or section of the tendons. The application of mechanical appliances and supports has also been recommended. A tight-fitting belt or jacket in some cases seems to be helpful; but mechanical supports (irons, etc.) for the limbs are, in my opinion, useless or injurious

The patient should be carefully guarded against cold and exposure; for in this, as in all forms of chronic spinal disease, cold seems to exert a depressing influence upon the condition.

Amongst drug remedies, arsenic and strychnine are probably the most useful. The systematic use of hypodermic injections of strychnine deserves, I think, a much more thorough and extended trial in this disease than it has hitherto received.

It is important to note that in some cases of pseudo-hypertrophic paralysis some temporary improvement may undoubtedly be effected by judicious treatment. Under arsenic, strychnine and the faradic current, the patient represented in Plate LXXXVII. fig. 3 undoubtedly improved. At the time of her admission to hospital she was quite unable to raise herself from the recumbent position; she could get into a sitting position and that was all. After two months' treatment, she could raise herself to the erect position with comparatively little effort or difficulty.

The internal administration of extract of thymus gland has been recommended in pseudo-hypertrophic paralysis In the few cases in which I have prescribed it, I cannot say that it has produced any beneficial effect. Two of the patients have slightly improved, probably I think in consequence of the arsenic, strychnine, massage and electricity which were simultaneously employed.

THE JUVENILE FORM OF MYOPATHIC MUSCULAR ATROPHY OR PROGRESSIVE MUSCULAR DYSTROPHY OF ERB

Although the juvenile form of progressive muscular atrophy usually commences in childhood or early youth, the average age at which it is developed appears to be somewhat later than that at which pseudo-hypertrophic paralysis commences. This form seems to begin much more frequently in later youth and early adult life than the pseudo-hypertrophic form. Females, too, are more frequently affected than in the pseudo-hypertrophic form.

The disease seems to run a slower and less active course than most cases of typical pseudo-hypertrophic paralysis. Many cases live for a long time, and some have been reported in which the patients have attained old age. In short, the tendency to kill is not so strong as in the pseudo-hypertrophic form.

In this form, as in pseudo-hypertrophic paralysis, the hereditary and family tendency is very strong.

The disease is characterised by a slow and gradually developed muscular weakness and atrophy, which in the great majority of cases tends to be progressive; and which is associated with enlargement, due either to a true or false hypertrophy, of certain muscles. But in the order of the development and the distribution both of the atrophy and the hypertrophy it differs from the more common pseudo-hypertrophic type. In typical cases of pseudo-hypertrophic paralysis, the weakness and atrophy commence in the legs and back, and the calf muscles are enlarged from pseudo-hypertrophy (lipomatosis). In Erb's juvenile form, the atrophy and muscular enlargement, in the earlier stages of the case at all events, chiefly involve the muscles of the shoulder and pelvic girdles.

In the upper extremity, the pectoralis major and minor (the clavicular portion usually excepted), the latissimus dorsi, trapezius, serratus magnus, rhomboids, biceps, brachialis anticus and supinator longus are usually atrophied; while the deltoid, infraspinatus and triceps are usually enlarged, often apparently as the result of an actual hypertrophy. The muscles of the forearm (with the exception of the supinator

longus) and hand usually escape or remain unaffected until the later stages of the disease.

According to Erb, well-preserved forearms, atrophied upper arms, hypertrophied deltoids and atrophied scapular muscles (the infraspinati excepted) are characteristic of this type.

In the lower extremity, the muscles of the hip and thigh, especially the glutei, the flexors of the hip and the extensors of the knee are usually atrophied. In the later stages, the muscles both on the front and back of the leg are often involved; but the calf muscles seem to be much less frequently affected during the earlier periods of the disease than in typical pseudo-hypertrophic paralysis.

In many cases, the muscles of the back (sacro-lumbalis and longissimus dorsi) are involved even in the early stage.

In rare cases, the facial muscles (chin and cheek muscles especially) are involved. The affection of the muscles of the face brings this form into relationship with the next type—the facio-scapulo-humeral type of Landouzy and Déjerine.

As a result of the muscular atrophy and wasting, deformities and lordosis are developed.

As in pseudo-hypertrophic paralysis, fibrillary twitchings are absent[1] and the reaction of degeneration is not developed.

The knee-jerk may be normal, diminished or lost, but is never exaggerated. There are no sensory symptoms; no affection of the bladder and rectum; and no visceral lesions. Further, as I have already so often remarked, our present methods of investigation fail to show any lesion either in the cord or in the nerves.

From this description, it will be seen that the disease is closely allied to pseudo-hypertrophic paralysis. There can, I think, be little doubt that the two diseases are mere variations of one primary form. I agree with Erb in thinking that the differences which the two types present, as regards the distribution of the atrophy and hypertrophy, the order of development and the varying degrees of intensity of the muscular lesions, are not of themselves sufficient to prove that the two conditions are fundamentally distinct. But I need not again discuss this important point. The mere fact that it is sometimes extremely difficult to say under which variety a special case should be placed, shows the close relationship which the different forms bear to one another.

As Sachs has pointed out, the juvenile form of Erb is much less frequently met with than the typical pseudo-hypertrophic form.

The later age at which the disease usually commences, its longer duration, its lesser tendency to kill and the greater frequency with which females are affected may all probably be explained by the lessened intensity which the disease presents. I have already stated that when pseudo-hypertrophic paralysis develops late, it is apt to be less severe; and that, in the female, the disease usually develops later and is less severe than in the male.

[1] On this point, see page 79.

Diagnosis.—The diagnosis of the juvenile form of progressive muscular atrophy is usually easy, provided that the observer is acquainted with the characters which this and the other forms of myopathic atrophy present. The fact that several members of the same family (brothers and sisters of the patient) are affected, or that other cases of a similar or allied nature have occurred amongst the patient's relatives (in his cousins, uncles, aunts, grandparents, etc.) is of great diagnostic importance.

The combination of atrophy and hypertrophy, and especially the peculiar distribution which the atrophy and hypertrophy present—well-preserved hand and forearm muscles, atrophied upper arms, enlarged deltoids and infraspinati and atrophied scapular muscles—are highly characteristic. The absence of fibrillary tremors and of the reaction of degeneration, diminished mechanical irritability and diminution or abolition of the deep reflexes are also of great importance.

From the pseudo-hypertrophic form, Erb's juvenile type is distinguished (though it must be remembered that this is not constant for in the juvenile form the calves may also be enlarged) by the absence of enlargement of the calf muscles, by the fact that the upper extremity is first affected, and by the peculiar way in which the atrophy and hypertrophy are distributed in the muscles of the shoulder girdle and upper limb. But I repeat that the two diseases seem to run insensibly one into the other; and that connecting types and irregular forms occasionally occur.

Prognosis.—Speaking generally, this seems to be more favourable than in the pseudo-hypertrophic form. Different cases differ, however, very markedly as regards their severity. In some, the course is rapid, in others, very chronic. As I have already said, some patients live on and reach old age. In others, the atrophic process seems to be arrested after a certain stage; but it must be remembered that in such cases a redevelopment may occur after an interval of quiescence and apparent arrest.

In trying to form an opinion as to the severity in any particular case, the age at which the disease develops, the rapidity with which the atrophic process is progressing, the number of muscles which are affected, and especially the condition of the respiratory muscles and of the diaphragm are the most important points.

In those cases in which the disease is developed early the course is usually more rapid and severe than in those in which the disease commences later.

Treatment.—The same methods of local and general treatment which have been recommended for the treatment of pseudo-hypertrophic paralysis are advisable.

THE FACIO-SCAPULO-HUMERAL TYPE OF LANDOUZY AND DÉJERINE

This is identical with the infantile form of progressive muscular atrophy of Duchenne. As I have already stated, it seems to be merely a modification of Erb's juvenile form and of pseudo-hypertrophic paralysis. Its peculiarity consists in the fact that the facial muscles are affected, and that they are (usually) the first muscles which are involved.

In this country, this type of the disease seems to be extremely rare. One case only has come under my own observation. This form also seems to be very rare in Germany, for Erb with his immense experience does not seem to have met with a single typical example of it. It would appear to be much more common in France.

In this form, the disease usually develops in childhood or early youth. Like the other forms of myopathic atrophy, it presents a strong hereditary and family tendency.

The affection of the facial muscles, when advanced, gives a peculiar appearance to the patient which has been termed the *facies myopathique*. The face is flattened, dull and expressionless; the lips, more particularly the lower lip, appear to be enlarged; the lower lip is everted (pouting); the mouth has been compared to that of a tapir (*bouche de tapir*). When the patient smiles, the angles of the mouth are not raised, but the mouth is drawn out transversely (*rire en travers*). The pronunciation of labials is more or less interfered with. The patient is unable to whistle (see Plate LXXXIX. fig. 4). When the disease is advanced, the wrinkles on the forehead may be completely effaced; in some cases, the orbicularis palpebrarum is so markedly affected that the eyes cannot be closed even during sleep.

In addition to the affection of the facial muscles, some of the muscles of the shoulder girdle and of the pelvic girdle are usually affected, as in Erb's juvenile form. Ultimately, almost all the muscles of the body may become involved.

Diagnosis.—When the affection of the face is advanced, this type is easily recognised by the peculiar expression, the char of the smile and the tapir-like form of the mouth. The e age at which the disease is developed is also in most case important aid to diagnosis.

When the facial muscles are only affected in a slight deg the atrophy may easily escape observation. And here I r say that it is of great importance to examine the conditio the facial muscles in all cases of suspected myopathic atro (pseudo-hypertrophic paralysis, Erb's juvenile form) with greatest care, not only during life but also after death. Po mortem observation has shown that, in some cases in which t face appears to be perfectly normal during life, the fac muscles are actually involved. This (unobtrusive) implicati of the facial muscles in the pseudo-hypertrophic and juveni forms, speaks strongly in favour of the view that the thr types are merely modifications of one and the same disease.

Prognosis.—This seems to be more unfavourable as regard rapidity of progress and duration than in the juvenile form Erb, but perhaps more favourable than in typical cases pseudo-hypertrophic paralysis.

Treatment.—The same as for pseudo-hypertrophic paralysis

THE HEREDITARY FORM OF PROGRESSIVE MUSCULAR ATROPHY OF LEYDEN

In this form, which is merely a modification of pseudo-hypertrophic paralysis, the weakness and atrophy usually commence in the muscles of the legs and back. In some cases, the calf muscles are enlarged or relatively enlarged in proportion to the atrophied condition of the thighs. Lordosis similar to that which characterises pseudo-hypertrophic paralysis is a striking feature. In some cases, the gait is very similar to that of pseudo-hypertrophic paralysis, but this is by no means always the case; and the same peculiar method of rising from the recumbent to the erect position (climbing up the thighs) is observed.

The hereditary tendency is strongly marked; hence the term, the *hereditary* form of progressive muscular atrophy, which Leyden applied to the disease. Several members of the same family are often affected. Fibrillary tremors and the reaction of degeneration are almost invariably absent, and the small muscles of the hand are usually spared until, at all events, the later stages of the case.

The disease usually develops in childhood or early youth, though generally at a later age than pseudo-hypertrophic paralysis. The course seems, as a rule, slower than in typical cases of pseudo-hypertrophic paralysis, for the intensity of the disease seems less. The case represented in Plate LXXXVII. fig. 6 falls under this type.

THE (PURELY) ATROPHIC FORM OF MYOPATHIC MUSCULAR ATROPHY

Cases are occasionally seen, but they are probably very rare, in which progressive muscular weakness and atrophy are developed, and in which there is no muscular hypertrophy. The muscles of the back and leg are usually first affected, but ultimately the atrophy may involve almost all the muscles of the body. In these cases, the characteristic lordosis and the same method of rising from the recumbent to the erect position is seen as in the pseudo-hypertrophic form. The gait is in some cases peculiar, but not exactly identical with that of typical pseudo-hypertrophic paralysis; it is not so waddling. I am in the habit of terming it the 'spider-crab' gait.

When the patient is stripped, the great tenuity of the limbs in proportion to their length, is a very striking feature. In particular, the thighs appear to be atrophied; the calf muscles, though not actually increased in size, usually, so far as my experience enables me to judge, appear to be relatively large. It is not improbable that in many of these cases (as in that represented in Plate LXXXVIII. figs. 4 and 5) the calf muscles are actually in some degree enlarged, or that they were enlarged prior to the time when the patient comes under observation.

This type seems to be identical with the form previously described (Leyden's form). The case represented in Plate LXXXVII, fig. 6 might be placed either under this form or under the type described by Leyden.

As I have already pointed out, the girl represented in Plate LXXXVII, figs. 3 and 4 is one of a family of six children, two

boys and four girls; two of the boys and two of the girls are affected. In the other three cases in this family, the disease presents the usual features of the pseudo-hypertrophic form. The identity of the hereditary form of progressive muscular atrophy of Leyden and the ordinary pseudo-hypertrophic form is conclusively proved by these cases. In the girl's case, there has never been any enlargement of the muscles, except perhaps of the glutei, for the buttocks look relatively large and are elastic and firm to the feel. Another point of great interest is that in this girl's case fibrillary tremors in the muscles of the back were very noticeable. In another case, which is represented in Plate LXXXIX, fig. 4, definite and distinct fibrillary twitchings were also seen.

Diagnosis.—When cases of this kind occur in an isolated form, the difficulty of diagnosis may be very great, unless the observer is well acquainted with the modifications which myopathic atrophy may present. These cases seem to be a mere modification of the pseudo-hypertrophic form. They are pseudo-hypertrophic paralysis without pseudo-hypertrophy.

The differential diagnosis of the purely atrophic form of myopathic atrophy and of the myelopathic (Aran-Duchenne) type of progressive muscular atrophy.—From the Aran-Duchenne type of progressive muscular atrophy, these cases are distinguished by:—The early age at which the disease develops; the fact that several members of the same family are usually affected, either with this or one of the allied forms of myopathic atrophy; the hereditary tendency which the disease usually presents; the absence of fibrillary tremors and of the reaction of degeneration; the diminution or abolition (never exaggeration) of the knee-jerks; the lordosis; the peculiar method of rising from the recumbent to the erect position; and the distribution of the atrophy and its order of development, for the small muscles of the hand are rarely if ever involved until the later stages of the case.

The differential diagnosis of the purely atrophic form of myopathic atrophy and the peroneal type of the disease.—These two forms can usually be differentiated without difficulty. In the peroneal type of the disease the foot and leg muscles are first affected, and then, after (usually) a considerable interval of time, the atrophy involves the small muscles of the hand, producing the characteristic *clawed* appearance.

The differential diagnosis of the purely atrophic form of myopathic muscular atrophy and the generalised progressive muscular atrophy of early childhood.—These conditions present many points of similarity, but I doubt whether they are the same disease. So far as my experience enables me to judge, the condition which I term the generalised progressive muscular atrophy of early childhood differs from the purely atrophic form of myopathic atrophy inasmuch as:—(a) it commences at an earlier age; (b) the atrophy is much more generalised (diffused); (c) the course is more rapid; ? (d) fibrillary twitchings and the reaction of degeneration are usually present; and (e) the nerve cells in the interior cornua of the spinal cord and the peripheral nerves (if the case reported by Drs. Thomson and Bruce may be taken as a type) are distinctly affected (atrophied and degenerated).

The Course, Prognosis, and Treatment are the same as in pseudo-hypertrophic paralysis.

GENERALISED PROGRESSIVE MUSCULAR ATROPHY OF EARLY CHILDHOOD

Cases are occasionally met with in which a generalised (diffuse) muscular atrophy, which has not the distribution of that which is characteristic of any of the preceding types and which is unassociated with any muscular hypertrophy or pseudo-hypertrophy, is developed in early childhood. These cases ought, I think, to be placed in a separate group. They would appear to be very rare. They seem to me to be very closely allied to, probably identical with, the subacute inflammation of the anterior cornual region described by Duchenne under the term *paralysie générale spinale antérieure subaigue*.

Through the kindness of Dr. John Thomson, I had the opportunity of seeing a characteristic example which he has described, with full pathological report by Dr. Bruce.[1] Another case came under my own observation a few months ago.

In Dr. Thomson's case (see Plate LXXXIX, figs. 5, 6 and 7) the clinical features were as follows:—

The patient, a young, most intelligent female child, who presented no hereditary tendency to the disease, suffered from profound paralysis and considerable muscular wasting which affected in a varying degree most of the voluntary muscles of the body. The paralysis began insidiously and without known cause, probably when the child was between 12 and 18 months old. The onset of the paralysis was unaccompanied by fits, pain, or febrile disturbance; it seemed to have developed subacutely in the lower limbs, which were severely affected for at least a year before the upper ones were affected. After an interval, during which little change was noticed in the lower extremities, the upper limbs and neck became rapidly (within three to four weeks) weakened. The face was never more than very slightly affected.

The wasting developed gradually, and not nearly so rapidly as that of ordinary poliomyelitis anterior acuta. Further, the atrophy was progressive.

In the earlier stages of the case, the muscular weakness seemed out of all proportion to the wasting.

The child lived for five years after the disease developed; during this period, the atrophy continued to advance steadily but very slowly.

The distribution of the wasting and paralysis was quite symmetrical, the lower half of the body being much more severely affected than the upper.

There was never any hypertrophy or pseudo-hypertrophy.

Fibrillary twitchings were seen in some of the muscles, especially in those of the face. Some of the muscles of the lower limbs became slightly shortened (contracted), and the joints distorted (see Plate LXXXIX, figs. 6 and 7). The muscular co-ordination was unimpaired.

In the earlier stages of the case, the faradic excitability was much less impaired than the galvanic; later, the excitability to both forms of current was more equally affected (diminished); and, finally, the galvanic excitability was more impaired than the faradic. Distinct 'reaction of degeneration' was never found.

After the disease had lasted more than a year and a half, cramp-like pains were complained of. The sensibility to the pain produced by the application of faradic electricity was most curiously deficient. In all other respects the sensibility was normal.

There was never any affection of the bladder or rectum, nor any tendency to the formation of bed-sores.

[1] *Edinburgh Hospital Reports*, vol. i. page 372.

Twenty months before death almost total collapse of the left lung occurred suddenly during an attack of slight bronchitis, evidently favoured by the extreme muscular debility.

On post-mortem examination, the muscles presented a variety of appearances which closely corresponded with those described by Erb as characteristic of progressive muscular dystrophy. Some of the muscular fibres were atrophied, others hypertrophied. In places, there was a great increase of the nuclei of the muscles and of the sarcolemma. Many of the muscular fibres were split in a longitudinal direction; others presented vacuolations. There was some pseudo-lipomatosis.

In the nerves, there were quite a number of round and spindle cells between the fibres. Many of the nerve bundles were compressed and atrophied and even replaced by fibrous tissue.

In the spinal cord, a large number of the cells of the anterior horn had entirely disappeared; while the majority of those which remained had undergone atrophy to a greater or less extent.

The case is one of great interest and rarity. It is perhaps difficult to express a decided opinion as to its nature, but I agree with Dr. Bruce in thinking that it was probably myelopathic rather than myopathic. The following facts seem to support this view:—The onset was more rapid than in most cases of myopathic atrophy; the muscular wasting seemed to be preceded by muscular weakness (paralysis); fibrillary tremors were present; the galvanic excitability was in the later stages much more marked than the faradic; there were definite alterations in the peripheral nerves and in the spinal cord.

It has been suggested that in cases such as this in which the symptoms during life are suggestive or indicative of myopathic atrophy but in which the multipolar nerve cells in the anterior cornua of the spinal cord are atrophied and diminished in number after death, the atrophy and disappearance of the nerve cells is a secondary result of the peripheral muscular wasting. With this opinion I cannot agree. The remarkable case which is represented in Plate LXXXVIII, figs. 1 and 2 completely disproves it. In that case, the muscles had for years been in an extreme condition of atrophy, but the multipolar nerve cells in the anterior cornua were very numerous and large; their processes were very distinct; the only change which they exhibited was a certain degree of fatty degeneration.

In my own case, the symptoms, mode of onset and course were very similar. The patient was unfortunately seen only once and the case was not exhaustively investigated. Amongst other points, the electrical condition of the muscles was not ascertained. The history of the case is briefly as follows:—

Case of Progressive Muscular Wasting in a Young Child.—J. B., aged $1\frac{1}{2}$, was seen at the Edinburgh Royal Infirmary on March 31st, 1893, suffering from diffuse muscular atrophy.

Previous History.—The patient was a first child; his head was not injured at the time of birth; the labour, though long, was quite natural; instruments were not used.

The child seemed to be perfectly healthy during infancy; he grew and developed well, and nothing was noticed amiss with him until he was nine months old. He then began to lose the power of using his limbs. Up to this date, he seemed to be able to move his limbs as freely as any healthy child. Since the age of nine months, the muscular weakness and inability to move have slowly but gradually increased.

He has never been able to creep, stand or walk. His general health is now, and has always been, quite good. He has never had any illness.

Present condition.—The patient was a well-grown, well-developed child. He had several teeth. The appetite was good. He was a very intelligent child; his mother said that he was mentally more advanced than most children of his age.

The muscles generally were very soft and flabby.

During the whole examination, the patient lay perfectly helpless. He could move his toes and fingers a little, but was unable to draw up his legs or to put his arms to his head. The fingers were pointed, and tended to be hyper-extended. The muscles of the arms and legs were very flabby, soft and markedly wasted. The deltoids in particular were extremely atrophied; and the lower part of the pectoralis major seemed to be wanting. The muscles of the back were also markedly atrophied.

The knee-jerks were absent.

The electrical condition of the muscles was unfortunately not tested. The child was seen only once; he lived in the country at a considerable distance from Edinburgh; and although the parents promised to bring him back and have him admitted as an in-patient, they withdrew from this decision and could not be persuaded to bring the child back to the Infirmary.

There was no vasomotor mottling of the skin.

The sensory functions were perfectly normal. There was no affection of the bladder or rectum.

The heart and other organs were all healthy. The body was covered with a considerable quantity of subcutaneous fat.

Family History.—The parents were healthy, robust country people; no case of a similar kind had ever, so far as they knew, occurred amongst any of their relatives.

Diagnosis.—The case appeared to me to be very similar to the case described by Drs. Thomson and Bruce. Accordingly, after examining the patient, I sent him on to Dr. John Thomson, but without giving any indication as to what I thought of the nature of the condition. Dr. Thomson wrote me as follows —'It is a most interesting case, I never saw one exactly like it, but I think it has more points of resemblance to that of the little girl which Bruce and I are publishing in the Hospital Reports than to anything else that I have seen. Many of your patient's symptoms are just the same, but his back and arms are more severely affected than in our case. If I am not mistaken, the lower part of the pectoralis major is deficient or wanting; in our case it was very distinctly present. I should be inclined to diagnose the case as one of progressive muscular dystrophy, whether with or without a spinal lesion I do not know.'

Duration and course.—The patient remained much *in statu quo* until February, 1894, when he died after four days' illness from acute pneumonia. Dr. MacAllister, who had done his best to persuade the parents to bring him to Edinburgh, informed me that the trunk and leg muscles gradually became more atrophied and flabby, but that there seemed to be some improvement in the condition of the arms; for a few months previous to death, the patient had been able to use his arms and hands a little more than he had been able to do previously.

A post-mortem examination was not allowed.

THE PERONEAL TYPE OF PROGRESSIVE MUSCULAR ATROPHY

Dr. Tooth has applied this term to certain cases of muscular atrophy in which the muscular atrophy begins in the small muscles of the leg. Charcot, Marie, Hoffmann and others have described similar cases. Hoffmann has proposed the term '*progressive neurotic atrophy*'; and the disease is sometimes termed '*the Charcot-Marie type of progressive muscular atrophy.*'

The disease is very rare; one case only has come under my own observation. Its exact pathology is not as yet definitely understood; but it undoubtedly seems to be quite distinct from the cases of myopathic atrophy which I have just described. The clinical features of the disease seem to show that the lesion is situated either in the peripheral nerves or in the spinal cord. The atrophy is consequently either neuropathic or myelopathic.

As a rule, the disease begins in later childhood, youth, or

early adult life. Males are more frequently affected than females; but the tendency to affect males in preference to females is less marked than in pseudo-hypertrophic paralysis.

In a considerable proportion of cases, the disease seems to be hereditary, or to attack several members of the same family; isolated cases are probably more frequent than isolated cases of the myopathic forms of atrophy. In some cases the disease has followed an attack of measles.

The course of the affection is very chronic. The atrophy commences in the muscles of the foot or leg. The extensor hallucis pollicis is usually first affected; then the extensors of the toes, the peronei and the small muscles of the foot are involved. It is not improbable, however, that in many cases the small muscles of the foot are affected at the very commencement, for weakness and atrophy in these muscles are much less easily detected than in the muscles of the leg, and are, therefore, apt to escape attention.

The atrophy is developed slowly and gradually and is progressive. After a time, the calf muscles become affected, and a characteristic deformity—talipes varus—which is due to weakness of the peronei muscles is developed.

After the atrophy has existed for some time (it may be three or four years or even longer) in the lower extremities, the muscles of the upper extremity become involved. The small muscles of the hand (thenar and hypothenar muscles) and the muscles of the forearm are first affected; and the bird-claw appearance of the hand which is so characteristic of the Aran-Duchenne type of progressive muscular atrophy is produced.

The muscles of the thigh, upper arm, pelvic and shoulder girdles, back, trunk and neck, may ultimately become involved.

The atrophy is usually but not always symmetrical. In the first case, for example, reported by Tooth in his memoir on the subject, the muscles of the right leg were markedly atrophied, while those of the left were scarcely affected. There is never any muscular hypertrophy or pseudo-hypertrophy.

Fibrillary or fasicular muscular twitchings frequently occur, and the reaction of degeneration in its imperfect form is usually developed. Myalgic pains occasionally occur, and various derangements of sensation are also sometimes observed.

It is obvious from these characters that the type of disease is peculiar. It resembles the Aran-Duchenne type in the facts that the muscles of the distal end of the affected extremities are first involved, and that fibrillary twitchings and the reaction of degeneration are developed. But it differs from the Aran-Duchenne type inasmuch as the atrophy begins in the muscles of the foot and leg, that the disease usually commences in childhood, youth, or early adult life, and that in many cases it presents the hereditary and family tendencies which are so characteristic of the myopathic forms of muscular atrophy.

As yet, very few cases have been examined post mortem. In two at least, changes in the peripheral nerves, without any corresponding lesions in the anterior cornua of grey matter, were present. But it is perhaps, as yet, premature to conclude that the lesion is neuropathic. As Sachs has pointed out, the clinical features of the disease closely correspond to those of progressive muscular atrophy of the Aran-Duchenne type. Sachs indeed proposes to term the disease '*the leg type*' of progressive muscular atrophy. Further pathological observations are required in order to settle this disputed point.

Diagnosis.—When well advanced, the disease is easily recognised. The bird-claw condition of the hands, when combined with talipes varus and atrophy of the muscles of the leg and foot, is highly suggestive. If, in a case of this kind, it is ascertained that the atrophy commenced slowly and gradually in the muscles of the foot and leg and subsequently extended after a considerable interval to the muscles of the hands and forearms, the diagnosis of the peroneal type of progressive muscular atrophy may confidently be made.

Prognosis.—The course of the disease is slow and chronic, but, so far as our present knowledge enables us to judge, usually progressive.

Treatment.—The same treatment which has been recommended for the Aran-Duchenne type of progressive muscular atrophy should be employed. An elastic bandage and stiff boot are advisable in order to counteract the foot deformity.

POINTS TO BE OBSERVED IN THE CLINICAL EXAMINATION OF CASES OF PSEUDO-HYPERTROPHIC PARALYSIS AND OTHER FORMS OF PROGRESSIVE MUSCULAR DYSTROPHY.

Preliminary Facts.—Name; age; sex; occupation; address; date of examination; birthplace; social circumstances and surroundings.

Previous History.—(1) *Prior to the present illness.* Condition at birth. State of health up to the time at which the first symptoms of the disease were noticed. Details of any illnesses which the patient may have had during this (preliminary) period. Age at which the patient commenced to walk. Whether anything peculiar was observed in his manner of standing, walking, running, jumping, going upstairs, getting up from the ground, etc., prior to the time at which the first symptoms of the disease were noticed.

(2) *History of the present illness.* The date and age at which the first symptoms of the disease were noticed. Nature of the first symptoms. Mode of onset (slow and gradual, etc.). Whether there was any apparent or supposed cause for the disease, such as an acute febrile disease (measles, scarlet fever, sore throat, diphtheria, epileptic fits), traumatic injury, fall, etc. The exact character of the symptoms and the order of their development since the disease was first noticed.

Family History.—Ages of father and mother, brothers and sisters; their condition of health; whether any of them are, or have been, similarly affected; whether any cases of a similar nature have occurred in previous generations (grandparents, uncles, aunts, etc.) or in collaterals (cousins).

A complete chart of the family should, if possible, be drawn up.

Present Condition.—Height, weight, general appearance and expression. Attitude in the erect position (lordosis, etc.). Gait.

Mode of rising from the recumbent to the erect position.

Ability to fix the shoulders against resistance.

The condition of the motor nerve apparatus.—The following points should be carefully noted:—

(1) *The patient's ability to perform different movements.*

(2) *The force with which movements are performed.*

(3) *The condition of the different muscles in respect to hypertrophy or pseudo-hypertrophy and atrophy.*

A detailed statement should be made of the condition of:—The muscles of the feet, legs (especially the calves), thighs, pelvic girdles (especially the glutei), back, abdomen, scapulæ, shoulder girdles (especially the infraspinati, deltoids, lower parts of the pectoralis major and latissimus dorsi), upper arms, forearms (especially the supinator longus), hands (especially the interossei, thenar and hypothenar), face, neck, tongue, etc.

In cases of the facio-scapulo-humeral type, the presence or absence of the '*bouche de tapir*,' '*sourire en travers*' should be noted.

Measurements. A detailed measurement should be made of the limbs, etc. (length, breadth), especially of the relative size of the calves, thigh, and of the arms and forearms respectively.

(4) *The condition of the atrophied and enlarged muscles* as regards:—(a) Motor power; (b) firmness, rigidity, tension and contractures; (c) the presence of fibrillary tremors; (d) the condition of the electrical reactions (the effect of the faradic and constant current, simple diminution, presence of the reaction of degeneration); (e) mechanical irritability; and (f) microscopical character of portions of muscle removed by incision or the harpoon.

The presence or absence of fibrillary twitchings and of the reaction of degeneration and the microscopic condition of the muscles are especially important from a scientific point of view.

(5) *The condition of the reflexes*, superficial and deep, and especially of the knee-jerks. The condition of the vesical and urinary reflexes.

(6) *The condition of co-ordination and the muscular sense.* The condition of the muscular sensibility to painful and electrical stimuli.

Vasomotor and trophic derangements.—The trophic condition of the skin, bones, joints; the presence of venous mottling of the skin, blueness and coldness of the hands or feet, etc.

The condition of the sensory nerve apparatus.—The condition of the sensibility of the skin to touch, heat and cold, and to electrical stimuli. The presence of myalgic or other pains in the affected limbs, joints, etc. The condition of the special senses.

Mental functions.—The condition of the intellectual faculties, memory, mental development, etc.

The condition of the other organs and systems.—(Circulatory, respiratory, digestive, urinary, etc.). In the case of males, whether the genital organs are naturally developed; in the case of females, whether the menstruation is regular and natural.

Progress and Course.

Treatment and its Results.

Total Duration.

Post-mortem Examination.—The following points should be carefully examined:—

(1) The condition of the *affected muscles* as regards:—
- (a) Naked-eye characters.
- (b) Microscopic characters (especially the presence or absence of enlarged and hypertrophied muscular fibres, lipomatosis, vacuolation or splitting of the muscular fibres, increase of nuclei in the sarcolemma or of the muscle fibres; and the condition of the blood vessels).

The condition of the intra-muscular nerves and nerve-endings. This is of special importance from a scientific point of view.

(2) The condition of the *peripheral nerves.*

(3) The condition of the *spinal cord, spinal membranes* and *nerve roots* (especially the presence of malformations, fissures, softenings and the number and appearance of the multipolar nerve cells in the anterior cornua and the condition of the anterior nerve roots).

(4) The condition of the *medulla oblongata, pons Varolii, cerebrum and cerebellum.*

(5) The condition of the *heart* (naked eye and microscopic), and of the *other organs.*

NOTES OF CASES OF PSEUDO-HYPERTROPHIC PARALYSIS AND OTHER FORMS OF PROGRESSIVE MUSCULAR DYSTROPHY

Case 1.—Typical Pseudo-hypertrophic Paralysis; Enormous Enlargement of the Infraspinati Muscles.

G. R., aged 11 years, 11 months; height 4 ft. 1 in.; weight 3 st. 11 lbs., was admitted to Ward 27, Edinburgh Royal Infirmary on 9th June, 1894, suffering from pseudo-hypertrophic paralysis.

Previous History.—The patient's mother states that he was a strong active child, able to run and jump as well as any boy, until he was 8 years old. At this time, he began 'to fall away' (get thin) and to run and move less actively than before. About a year later, his mother noticed that if he fell, he took a long time to get up from the ground and that 'he had to help himself up by gripping his knees.' After this date, the weakness rapidly increased; his gait became rolling, and his balance became so insecure that he fell over when pushed slightly to one side. About June 1893, a swelling of the shoulders (enlargement of deltoids and infraspinati) was noticed.

All these symptoms have gradually got worse, and for the last six months, he has been unable to get up from the floor.

The patient was a backward child; he was two years old before he began to walk, five years before he began to speak, and seven years of age before he was able to go to school. He is now mentally quite as quick as other boys of his age. He was quite healthy till the difficulty in walking commenced, He had measles and chicken-pox when he was four years of age. His present disease commenced without any apparent cause.

Family History.—The father, aged 50, is a strong healthy man; the mother, aged 39, is strong and healthy. A sister of the mother suffered from weakness in the legs, but she did not walk in the same way as the boy does. (The exact nature of the weakness in the legs in this aunt's case is uncertain.) The father's relations are all healthy and strong; none of them have suffered from any nervous complaint. So far as is known, no other case of pseudo-hypertrophic paralysis has occurred either amongst the father's or mother's relations.

There have been two miscarriages and four children in the family. The ages of the patient's brothers and sisters and the dates of the miscarriages are as follows:—

1. Miscarriage at 7th month.
2. The *patient*; boy aged $11\frac{11}{12}$.
3. Miscarriage at 5th month.
4. Girl, aged 10; quite healthy and strong.
5. Boy, aged 6; quite healthy and strong.
6. Girl, aged $2\frac{1}{2}$; quite healthy and strong.

It is of course quite possible that some of the other children may subsequently manifest the disease.

Present Condition.—There are several scars on the forehead and back of the head, the result of falls, and marks of old burns on both calves and on the inner side of the left knee. The face is full and plump about the cheeks; the forehead is somewhat narrow; the expression is rather stupid looking, but the patient is quite intelligent.

Both deltoids are enlarged and prominent. The sternal portions of the pectoralis major on both sides are atrophied. The infraspinati muscles are enormously, and the supraspinati slightly, enlarged. The rhomboids are atrophied. The latissimus dorsi is also enlarged and forms a swelling round the angle of the scapula both below and in front. The buttocks and calves are considerably enlarged. The flexors of the thigh are enlarged. The heels are slightly drawn up by contraction of the tendo Achillis. The extensors of the legs are fairly large. The calf muscles are markedly enlarged.

Temperature on admission was subnormal.

Attitude in the erect position. When placed in the erect position

the patient is able to stand quite steadily and to maintain his balance The back is markedly curved forwards in the lower dorsal and lumbar regions, the chest and abdomen are thrown forwards and the shoulders backwards (see Plate LXXXVII. fig 2), but a line dropped perpendicularly from the shoulders does not fall behind the buttocks

The feet are placed wide apart and the toes turned in.

The slightest push in any direction which disturbs the equilibrium is sufficient to knock the patient over, he is unable to regain his balance when his centre of gravity is disturbed ever so little, and if pushed forward or backward, however slightly, he falls with a flop to the ground.

Gait. The patient is able to walk with a waddling gait, swaying from side to side, and using his arms to balance himself In walking, the toes are turned in, the *right foot* is inverted and its big toe drawn up, the instep of this foot is highly arched, the left foot is placed flat on the ground.

Mode of rising from the floor. When the patient is laid on his back, he is able to get on to his feet but not to rise into the erect position, his manner of rising is quite characteristic. He first turns over on to his side, then gets on to his hands, then straightens his arms and raises his chest and gets on to his knees, he then raises himself by the usual series of manœuvres, climbing up his thighs with his hands, but he is unable to get into the erect position without assistance (see Plate LXXXIX fig 8).

With the help of a chair, he is able to climb into bed unaided

When one attempts to lift him by putting the hands in the axillæ, his shoulders go up to his ears The inability to fix the scapulæ to the thorax is well seen in Plate LXXXIX fig 3

Motor power All the movements of the lower and upper extremities can be performed, but the motor power of the muscles of the trunk, arms and legs is markedly impaired

The condition of the muscles The sternal portion of the pectoralis major is atrophied on both sides, the clavicular portions are very soft and flabby Both infraspinati are enormously enlarged, especially the left, they stand out as firm elastic swellings and feel like masses of indiarubber The supraspinati are also slightly enlarged A bulging or swelling is present on both sides below and in front o the angle of the scapula, it appears to be due to enlargement of the latissimus dorsi Both deltoids are markedly enlarged, and have the same firm elastic feeling as the infraspinati muscles The triceps on each side is enlarged The muscles of the upper arm are soft and somewhat atrophied. Those of the forearm are slightly enlarged and for the most part softer than normal The supinator longus on each side, especially on the right side, is enlarged The muscles of the hand are normal

Both buttocks are enlarged; they feel firm and elastic. The flexors and extensors of the thigh are enlarged and firm, when the patient is standing in the erect position a hollow is seen on the inner side of the thigh in the position of Scarpa's triangle, especially on the right side The calf muscles are very prominent The tendo Achillis is slightly contracted and the foot tends to assume the equinus position The calf muscles are markedly enlarged and firm The extensors of the leg are firm but normal in size The extensor proprius hallucis of the right foot is slightly contracted, and the big toe is in consequence semi-flexed

The right foot is inverted, its instep high; it is flattened from before backwards, and closely resembles the foot of Friedreich's ataxia. The left foot is flat, but not misshaped like the right.

The measurements of the limbs are as follows:—

		Inches
Forearm (thickest part),	right	$6\frac{3}{4}$
" "	left	$6\frac{3}{4}$
Upper arm "	right	$6\frac{1}{4}$
" "	left	$6\frac{1}{8}$
Round deltoid at upper fold of axilla,	right	$7\frac{3}{4}$
" " "	left	$7\frac{3}{4}$
Thigh (thickest part),	right	11
" "	left	11
Calf "	right	$8\frac{1}{2}$
" "	left	$8\frac{1}{4}$

The enlarged muscles are firm and elastic to the feel, there are no fibrillary tremors, the mechanical irritability is normal

The facial muscles do not respond freely to electricity The electrical irritability of the muscles of the limbs and trunk is also distinctly diminished to both forms of current. There is no reaction of degeneration

Reflexes The knee jerks are absent, there is no ankle clonus The plantar and epigastric reflexes are absent No reflexes can be elicited in the upper extremities The organic reflexes are normal.

Vasomotor and trophic condition of skin, etc The hands and feet tend to be blue and cold and there is some venous mottling of the skin

Sensory functions The sensibility of the skin to tactile, painful and thermal stimuli is normal, the sensibility to electrical stimuli appears to be diminished The special senses are normal.

Mental functions The patient can read fairly well, intellectually he seems to be up to the normal

The circulatory, respiratory and digestive systems are normal

Urinary system The urine occasionally contains a slight trace of albumin but is otherwise quite normal

Treatment The patient was kept in bed Strychnine and arsenic were given by the mouth, strychnine was injected subcutaneously, and the faradic current was applied daily to the atrophied muscles

Subsequent Notes At the end of six weeks the patient was discharged very much *in statu quo* He was perhaps a little stronger, but there was certainly no decided improvement

On July 18th, a portion of the left deltoid was excised, under chloroform, by Dr Cotterill Sections, which were kindly prepared by Dr Muir, showed the usual changes characteristic of the disease —large masses of fat cells between the muscular fibres, marked atrophy of many of the muscular fibres, decided enlargement of others and an enormous excess of nuclei and connective tissue The last feature was so marked that Dr Muir suggested that the portion of muscle which was excised seemed to have been close to the insertion of the muscular fibres with the tendon. The portion of muscle removed was from the centre of the deltoid, from that portion of the muscle which formed a firm elastic swelling

The individual muscular fibres were for the most part atrophied (a few were enlarged); the peripheral nerves were quite normal

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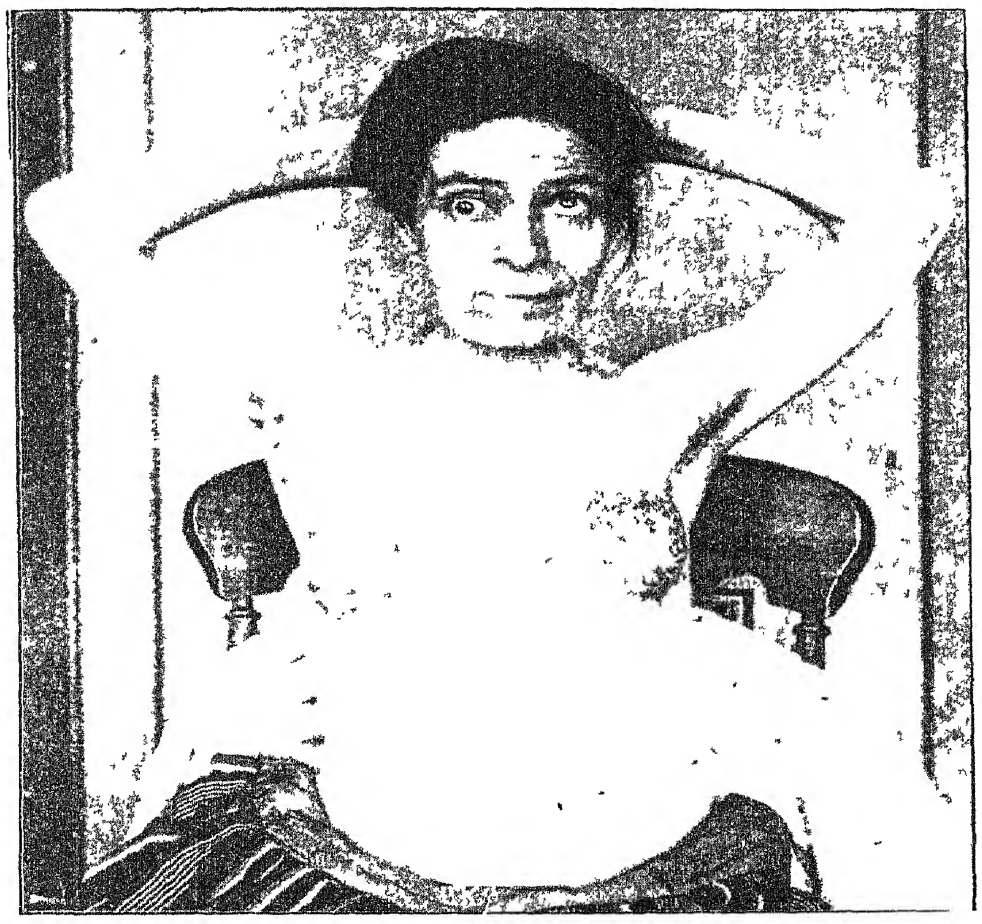
NOTE.—The next fasciculus will contain the clinical histories of several additional cases of pseudo-hypertrophic paralysis and other forms of progressive muscular dystrophy



CONGENITAL SYPHILIS.

FIG. 1.—Paralysis and atrophy of the tongue due to a syphilitic tumour at the base of the brain; tertiary ulcer on mother's arm.

FIG. 5.—Typical facies indicative of congenital syphilis.

FIG. 4.—Syphilitic teeth.—(After Jonathan Hutchinson.)

FIG. 2.—Syphilitic eruption of fœtus.—(After Ricord.)

FIG. 3.—Congenital syphilis: the patient represented in Plate LXXXI.

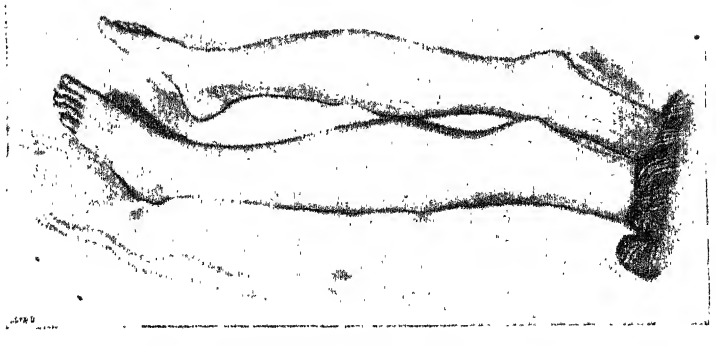


FIG. 6.—Congenital syphilitic disease of the tibiæ.

FIG. 1.—Congenital syphilis: healthy physiognomy.

FIG. 3.—The sister of the patient represented in Fig. 1 affected with epilepsy and syphilitic dementia (G. P.).

FIG. 6.—Congenital syphilis: extensive ulceration of skin of chest: a long, big-like process hangs from the ear.

FIG. 4.—Congenital syphilis: typical physiognomy: blood condition not significantly affected.

FIG. 2.—Ulcer of the palate, in the patient represented in Fig. 1.

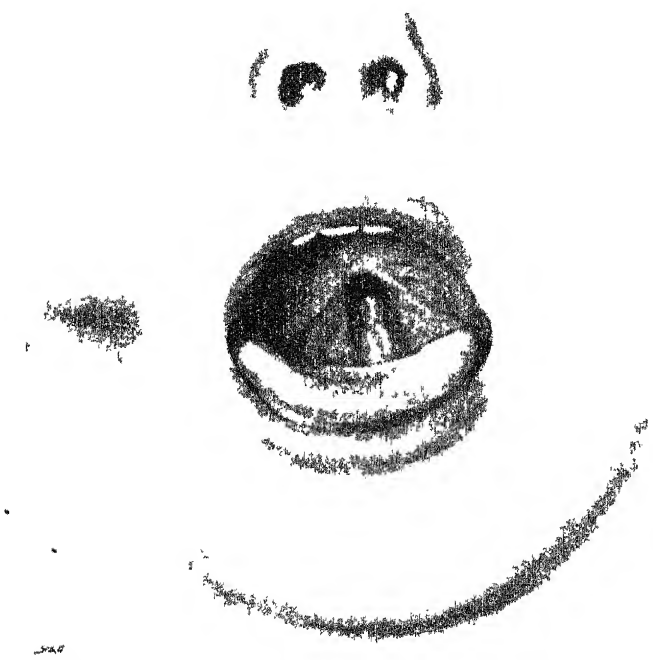
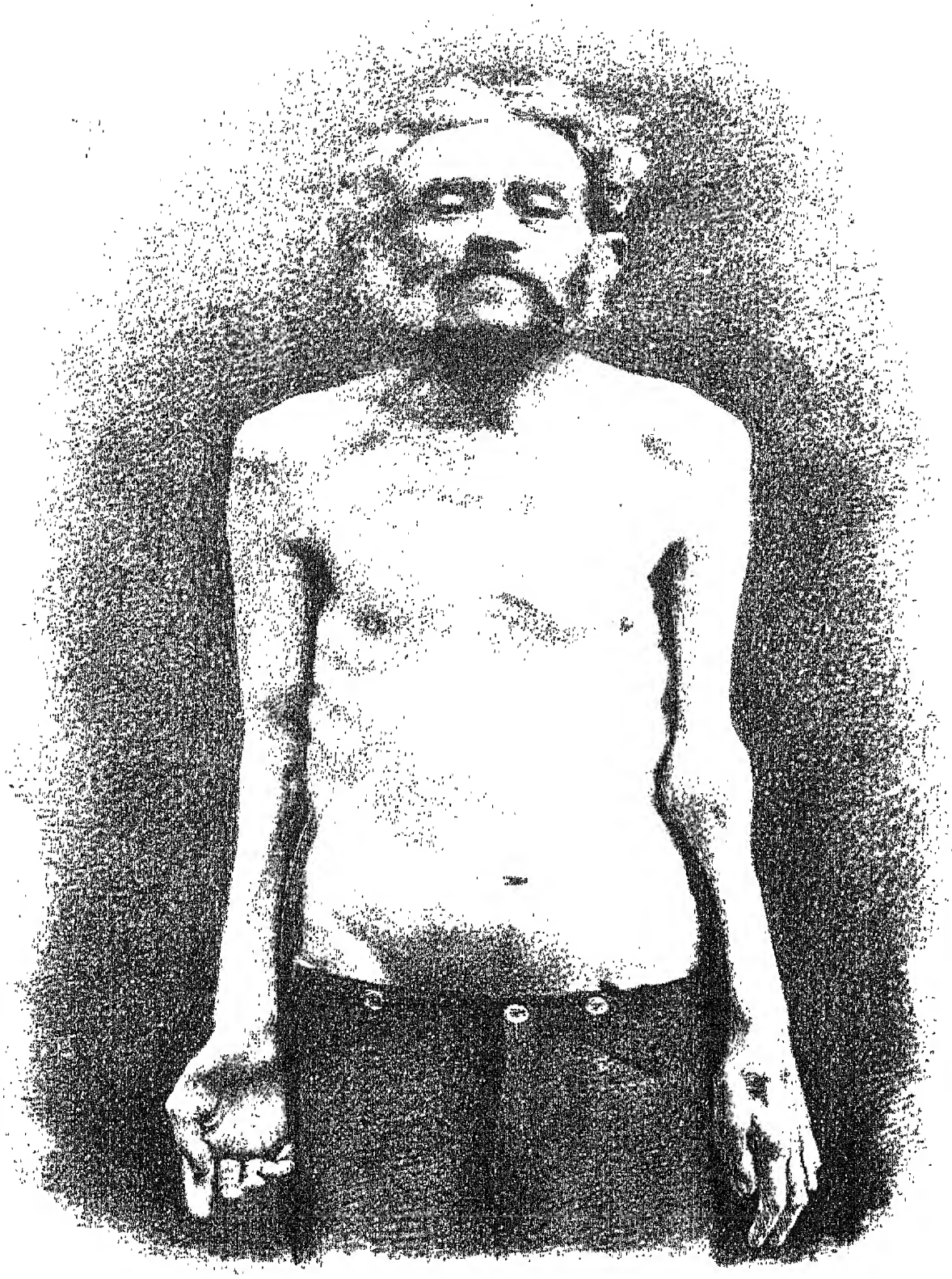


FIG. 5.—Extensive destruction of the palate in the patient represented in Fig. 4.



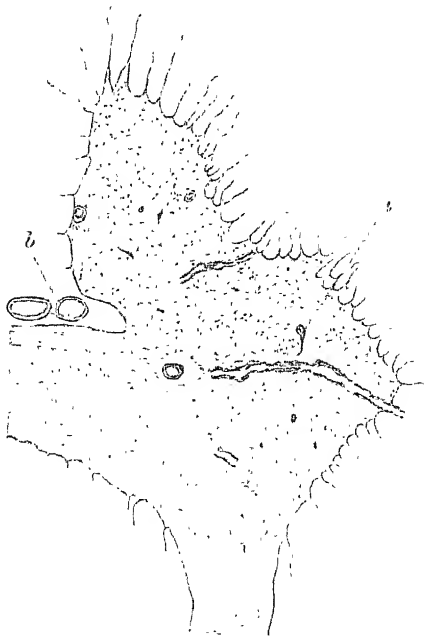


FIG. 1.—Anterior horn of grey matter in progressive muscular atrophy.

FIG. 2.—Anterior horn of grey matter from a healthy spinal cord, for comparison with Fig. 1.

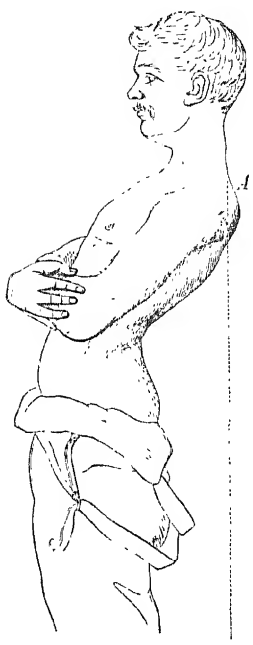


FIG. 7.—Atrophy of the lumbar muscles.

FIG. 8.—Typical case of progressive muscular atrophy.

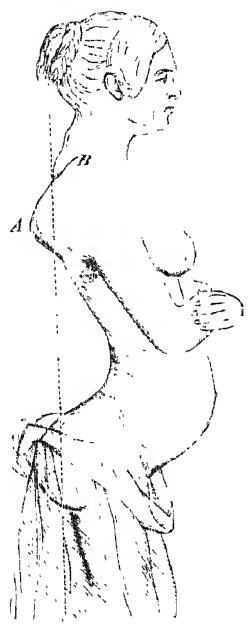


FIG. 6.—Atrophy of the abdominal muscles.

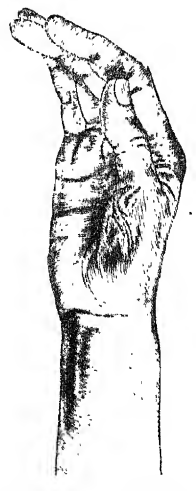


FIG. 3.—Wasting of the ball of the thumb.

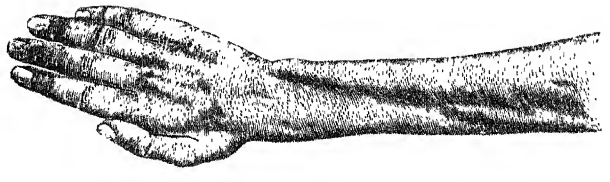


FIG. 5.—Atrophy of the forearm muscles.

FIG. 4.—Atrophy of the interossei and forearm muscles.

THE SPINAL FORM OF PROGRESSIVE MUSCULAR ATROPHY.

CASES OF PSEUDO-HYPERTROPHIC PARALYSIS AND OTHER FORMS OF PROGRESSIVE MUSCULAR DYSTROPHY

Case II. Typical pseudo-hypertrophic paralysis.

E S. J., aged 23, was seen in August 1891, with Dr. Alexander Wheeler.

Previous History —The disease seems to have been first noticed when the patient was about ten years of age. Dr. Wheeler states that as a child (up to the age of eight years) he was able to walk and run with other children, but was always slow in his movements and was consequently called 'Little lag behind' From infancy his calves were admired because of their large size. About the age of ten the difficulty in walking became more pronounced, but the nature of the disease was not recognised until hollowing of the back occurred. About this time the patient was seen by Dr. Gowers. Dr. Wheeler first saw him in 1885. He then presented all the typical characteristics of pseudo-hypertrophic paralysis. At this time he could walk two miles by himself. He was able to get up from a sitting posture, but he could not raise himself from the ground.

During the summer months he usually improved, while the muscular debility increased during the winter. This was more marked during the winter of 1888-89 than previously.

Since the year 1887 he has had pleurisy, tonsilitis, several attacks of bronchial catarrh and influenza. He seemed to recover from these diseases quite as well as other people.

Since the disease first commenced, he has been more or less continuously under treatment with massage and electricity; but the only time when there seems to have been any real improvement was during the winter of 1886 when Dr. Wheeler injected arsenic locally and applied massage more systematically than it had hitherto been employed.

Family History.—The patient has one brother and two sisters living. (Three brothers and one sister are dead; three died in infancy of ordinary diseases; one brother at the age of 24 from typhoid fever.) None of them are affected with pseudo-hypertrophic paralysis; and so far as is known, no case of the disease has ever occurred amongst any of his relatives. Two of the sisters are married; they have each had two children, none of whom have manifested any symptoms of the disease.

There is a history of gout both on the father's and mother's side. The patient's sisters have suffered from hysteria. While pregnant with the patient his mother had several severe frights.

Present Condition.—The case is in every respect a typical one of pseudo-hypertrophic paralysis. The calves are greatly enlarged; the right measures 14½ and the left 14 inches. The muscles of the thighs and buttocks are also enlarged, firm and hard. The latissimus dorsi and to some extent also the pectoralis major, biceps and triceps are atrophied.

The knee-jerks are absent. The plantar reflex cannot be elicited. The bladder and rectal reflexes are normal.

In the erect position the attitude is quite characteristic, the hollowing out of the back due to the antero-posterior curvature in the lower dorsal region being very marked. The chest is flattened from before backwards; the abdomen prominent. The gait is typical. Muscular co-ordination seems perfect; the patient is a fine violin player and a good artist. He has great difficulty in getting up from his chair and in going upstairs. He is unable to raise himself from the recumbent to the erect position.

The sensory functions, including the muscular sense, are normal.

Intellectually, the patient is much above the average. His memory is excellent; his temper somewhat fiery.

The general health is good and there is no visceral disease.

Treatment.—The patient was advised to continue the arsenic and strychnine, massage and faradic current which were originally prescribed by Dr. Gowers.

Subsequent Progress of the Case —During the winter of 1891 he was obliged to give up his violin playing, because he felt the violin too heavy. During the same winter he was laid up for some months with severe sprain of the ankle. Since then he has been gradually getting weaker, but was able to do a good deal of work in his father's office, drawing maps, etc. During the past year he has become decidedly worse.

On *6th October* 1896, Dr. Wheeler wrote me saying —'The bodily health is good, the patient is generally emaciated, the hypertrophied muscles less in bulk; the intellect is as bright as ever; he can still do a large amount of work in the estate office in which he is employed, by leaning far over the table when drawing maps, he cannot stand, so has to sit at his work He has run the gauntlet of double pneumonia, influenza, pleurisy with effusion, and severe diarrhœa, all within the past two years'

This last statement is a most remarkable one.

Cases III., IV., V. Typical pseudo-hypertrophic paralysis in the early stages, passing into extreme myopathic atrophy: Post-mortem examination in one case.

Cases IV and V. were seen with Dr. Felkin on 17th February 1893, they are of great interest because of the extreme muscular atrophy and the marked contractures which were ultimately developed (see Plate LXXXVIII Figs. 1 and 2).

Family History.—The patients belong to a family which originally consisted of seven children—three boys and four girls. All the boys have been affected and all the girls have escaped. The ages (in February 1893) were as follows:—

Case A. *Boy*, aged 18¾; *affected.*
Case B. *Boy*, aged 17½, *affected.*
C. Girl, aged 16; healthy.
D. Girl, aged 14; healthy.
E. Girl, aged 12, healthy.
F. Girl, aged 10; healthy.
Case G. *Boy*, aged 8; *affected*

No other cases of a similar nature have ever, so far as is known, occurred in any of the relatives.

The father was a healthy, tall, robust-looking man aged 47. He died at the age of 48 of acute croupous pneumonia. The mother is a stout, robust, active woman aged 46. She has always enjoyed good health. The grandparents, uncles and aunts on both sides have been healthy people. Several of the mother's brothers and sisters have large families, both boys and girls; none of the children (cousins of the patients) are affected with the disease.

One of the mother's brothers suffered for some years from, and ultimately died of, locomotor ataxia.

Two of the father's sisters are married. Both have children, all girls, all healthy.

The detailed notes of the cases are as follows:—

Case III. (Case A in this family.)—R. G., died at the age of 18¾ of pseudo-hypertrophic paralysis.

For several years before his death he was completely crippled. In the latter stages of his illness his condition was exactly similar to that of the second boy whose case is represented in Plate LXXXVIII. Figs. 1 and 2. All the muscles were extremely

atrophied. His arms were contracted at the elbow joints and his legs curled up under him, as in the second patient. His feet were in a condition of talipes equino-varus. His spine was curved.

The onset was gradual, without any apparent cause.

The difficulty in walking became very apparent when the patient was about 7 years of age, after an attack of measles; but the disease had evidently been in existence for some time previously, for he was stiff in his walking before this date. His gait at this time must have been typically that of pseudo-hypertrophic paralysis, for his mother says he walked in exactly the same way as his youngest brother (Case V.) now walks. At the age of 10, the muscular weakness became rapidly worse and he became unable to walk.

Mentally he was a sharp boy. He died from an attack of bronchitis. For some months before his death his bladder seems to have been affected, for his urine dribbled away.

In this case there was no post-mortem examination.

Case IV. (Case B in this family.)—C. G., the patient represented in Plate LXXXVIII. Figs. 1 and 2, was first seen with Dr. Felkin on 17th February 1893, and was subsequently examined on several occasions.

Previous History.—The difficulty of walking became marked after an attack of measles at the age of 6; the disease, however, seems to have been in existence before this date, for prior to the attack of measles the patient walked stiffly. He could never run and jump like other boys. After the attack of measles the difficulty in walking slowly but gradually increased. His mother says that at this time the gait was exactly similar to that of his younger brother (Case V.) who now (February 1893) presents all the characteristic features of pseudo-hypertrophic paralysis (see Plate LXXXVIII. Fig. 3). He completely lost his walking power about the age of 10. For some time previous to this, he was carried backwards and forwards to school. He was doing well at his lessons and was in the 4th Standard. When he first became affected the neighbours used to think that he was merely imitating his elder brother; the gait was exactly the same in the two cases.

Present Condition.—When first seen on 17th February 1893, the patient was a complete cripple. Almost all the voluntary muscles of the body were extremely atrophied, and there were marked contractures both in the lower and upper extremities (ankle, knee, hip, elbow). The patient was unable to feed himself. He could, however, use his hands and fingers quite well. The muscles of the neck and face did not appear to be affected. The tongue was decidedly larger than normal.

Measurements.—The detailed measurements of the limbs, etc., were as follows:—

	Inches.
Length of humerus from tip of acromion to tip of elbow	13
Length of ulna	10
Thickness of arm at thickest part	4¾
Forearm, middle	5¼
Wrist to tip of middle finger	7¾
Length of middle finger	4⅜
Circumference of ditto	2
Antero-posterior diameter of ditto	1
Circumference of hand	5¼
Circumference of head	21⅔
From occipital protuberance to root of nose	15⅛
From external auditory meatus to external auditory meatus	14⅓
Circumference of neck	12½
From tip of one acromion process to tip of other	11¾
Circumference of chest at level of nipple	28¾
Length of thigh	15¾
Length of fibula	12½
Length of foot	9⅛
Circumference of foot	8¾
Circumference of calf	7⅞
Circumference of thigh	8¼
Length of big toe	3¼

There were no fibrillary twitchings.

The atrophied muscles responded, though feebly, to the faradic current; the galvanic reactions were not tested.

The plantar reflex was absent.

The knee-jerks were absent.

The bladder and rectum were unaffected.

The sexual organs were fully developed.

The sensory functions were all quite normal.

The mental faculties were bright and active. The patient was a great reader.

The general health was good. The *digestive, circulatory, respiratory* and *urinary* organs were all normal.

The patient died on 3rd December 1893, from an attack of influenza and slight bronchitis.

Post-mortem Examination.—A limited post-mortem examination was made late at night by myself, on 5th December 1893. All the voluntary muscles were extremely atrophied; they looked more like fat than muscle. The cord was removed with great care in the usual manner and was at once placed in Müller's fluid, the membranes being left *in situ*. After it was sufficiently hardened and when I came to cut it up into suitable pieces for microscopical examination, I found that a deep fissure dipped down into the posterior horn of grey matter on the left side of the lumbar enlargement. Being anxious to get an absolutely independent opinion regarding it, I asked Dr. Muir to make the microscopical examination. He kindly did so. The following is his report:—

Dr. Muir's Report on the Condition of the Muscles and Spinal Cord in Case IV. (Case B in this Family.)

'*The Condition of the Muscles.*—The muscles showed the changes usually present in pseudo-hypertrophic paralysis, in a very advanced stage in some parts. On transverse section, it was seen that in many places the fasciculi of muscle-fibres had entirely disappeared, their place being taken by ordinary fatty tissue, whilst other fasciculi showed various stages of atrophy and lipomatosis. In these latter bundles the fatty accumulation was seen to begin generally at one side or towards the centre and spread in the form of a somewhat circular patch leaving a crescentic area of muscle fibres, which generally showed great variation in size. A varying amount of fibrous overgrowth was visible amongst the atrophying fibres, but this was by no means a prominent feature. The changes in the fibres were best seen, however, in longitudinal sections. These showed strands of fatty tissue, between which were lines of muscle fibres showing various changes. A few were enlarged, swollen and homogeneous, and often showing a proliferation of the nuclei of the sarcolemma; whilst others appeared as hypertrophied fibres with normal striation. Some of the latter were tortuous and crossed the plane of the section several times. Most of the fibres, however, showed various stages of atrophy; some were exceedingly small, some scarcely thicker than the diameter of a red blood corpuscle, but many, even of this size, showed quite normal striation, though a few were granular and degenerated. Amongst these small fibres was a varying amount of fibrous growth and accumulation of fat. The small fibres appeared to be formed in some cases by a simple atrophy, in others by a longitudinal splitting of the fibres attended by proliferation of the nuclei of the sarcolemma, which came to be arranged in rows. As the most extreme stage of atrophy, one could see bands of well nucleated fibrous tissue with a mere line of muscular substance in the centre recognisable only by its staining. Where growth of fibrous tissue took place along with the muscle atrophy it would appear this fibroid tissue also became infiltrated with fat after the muscle fibres had disappeared. The appearances would point to the changes in the muscle fibres as the primary change, the fibrous overgrowth and the lipomatosis being concomitants in varying degrees. (See Plate LXXXVI. Fig. 4; and Plate XC. Figs. 3 and 4.)

'*The condition of the peripheral nerves.*—The sciatic, anterior and posterior tibial nerves were examined and were found to be quite normal.

'*The condition of the spinal cord.*—The part of the spinal cord received was the lower lumbar and sacral portions. There were two longitudinal fissures. The higher fissure was about the lower end of the lumbar portion on the left side and entered at the posterior nerve roots, running directly forwards. The upper extremity was pointed, the lower somewhat blunted. It measured about half an inch in length and its margins appeared smooth. Almost immediately below this fissure was a second of about the same length. It was rather wider at its lower extremity where it entered the cord a little in front of the posterior nerve root, and on section could be seen to curve inwards to reach the posterior median fissure, thus enclosing with the latter a portion of the cord. This enclosed portion was largest below and diminished on passing upwards, the fissure gradually approaching the posterior surface.

'*Microscopical examination. Upper fissure.*—On making sections from above downwards, it is found that the fissure is visible in the

posterior horn before it reaches the surface. Examined at this level, the line of the fissure is seen to be antero-posterior, the anterior extremity reaching a little in front of the deep extremity of the anterior median fissure, the posterior extremity coming close to the surface at the entrance of the posterior nerve root. The anterior part of the fissure shows signs of mechanical extension; its margins are irregular, the surrounding tissue is opened up, whilst ganglionic cells with their processes are seen lying exposed and perfectly well preserved as regards form, etc. The fibres in the posterior nerve root at the posterior end of the fissure are somewhat broken up and separated. The intermediate (or middle) part of the fissure shows much more definite margins and the tissue around is distinctly condensed and stains more deeply. But while this is so, there is no very definite structural arrangement of tissue along the margin, no cellular proliferation as indicated by excess of nuclei, and no special arrangement of capillaries. One or two nerve cells can be seen close to the margin of the fissure, some of these appear imperfectly preserved or degenerated, whilst others appear normal. In one of the sections a ruptured capillary is seen crossing the fissure, the broken ends projecting from the two sides. At this level, the surface of the posterior column on the same side curves below the outline of the cord to the posterior nerve root, and the column is consequently considerably smaller on this than on the other side.

'At a lower level, the fissure reaches the surface and the posterior surface of the posterior columns curves with a bold sweep into the fissure, the left posterior column being still much smaller than the right. The margins of the fissure present much the same characters as described above. The fibres in the posterior cornu coming from the posterior root are cut obliquely across by the fissure. The surface of the posterior columns has been denuded of pia, but is smooth and regular. (See Plate LXXXVI. Figs. 2 and 3.)

'The nerve cells in the anterior cornua are numerous and absolutely healthy.

'*Nature of the fissure*.—What is the nature of the fissure? In favour of part at least being natural is the regularity of the margins and the condensation, and so much is this the case at places that it is difficult to conceive of its being produced by artificial means. But, on the other hand, so far as I can find after careful examination of the edges, there is no structural alteration which must necessarily be looked upon as *ante mortem*. The surface of the cord also shows signs of injury posteriorly, in the stripping of the pia, displacement of the nerve roots, etc. My impression at first was that there had probably been an elongated area of softening in the posterior cornu which had been artificially extended to the surface, but this supposition would not explain the condition of the left posterior column at the higher level described, i.e. before the fissure reaches the surface. At this level the left posterior column is much smaller than the right. It must either have been so naturally—which is not the case at higher and lower levels in the cord—or a portion must have been shaved off, when the pia was removed. So far as I can see, it is impossible to come to an absolute conclusion, but I do not think there is sufficient evidence from the sections alone to enable one to describe the changes as being undoubtedly *ante mortem*.

'As regards the *lower fissure*. After careful examination, I cannot look upon it as natural. In fact, I think all the appearances could be produced by force applied a little in front of the posterior nerve root and acting backwards. Such force might strip the pia, displace the nerve roots backward and cause a fissure or fracture into the posterior median fissure. At the upper part of this fissure there is a small rhomboidal space in the line of the posterior median fissure which at first suggests a loss of substance. But I think this may have been produced by the posterior part springing backwards.'

As I have already stated (see page 82) I feel great hesitation in expressing a positive opinion as to the significance of the changes which are present in these sections. That some of them are artificial I have little doubt, but that they are altogether due to this cause is by no means clear. I fail to see, for example, how the condition represented in Fig. 3, Plate LXXXVI., could be altogether the result of artificial damage. Dr. Muir takes a different view. After a very careful examination he concludes that there is no structural alteration which must necessarily be looked upon as *ante mortem*. Further, it will be noticed from Professor Sherrington's report (see p. 100) that the outlying cells in the white matter of the lateral and posterior columns are unusually numerous, and that in the tip of the lateral column there are little islets of gelatinous substance which are rarely, if ever, present in the normal spinal cord.

I was particularly struck with these peculiarities, and Professor Sherrington confirms my opinion that they are most unusual. They seem to suggest a congenital malformation of distribution of the cellular elements and gelatinous substance.

Feeling so much doubt as to the nature of the cord changes, I submitted the sections to Professor Sherrington, who has kindly sent me the following opinion regarding them:—

Professor Sherrington's Report.

'I have examined with interest the specimens of spinal cord received from you.

'The specimen was certainly well hardened, an important point in judging of the character of the fissure and cavity. I think some of these fissures offer the hardest problems in morbid histology.

'The appearance of a condensed edge can be sometimes given and closely resemble a sclerosed edge even in a purely artificial cavity. Some years back I made a number of artificial cavities in portions of spinal cord purposely by bending the pieces of cord at a not very sharp angle and tying them in that position and then hardening in Muller's fluid. The cavities obtained nearly always affected the posterior column and always ran into the grey matter opening there into a larger space. The sections through such ante-facts do not, however, agree in character with the appearances in your specimen. I do not think the cavity in your preparation explicable as an ante-fact.

'By hardening in bichromate we sacrifice the grey matter—except the borders of the coarser ganglion cells in it—for the sake of the white column. The spongiosa is shrunken much more than the white matter, as can be seen by its sunken level at the ends of a block of cord hardening in Muller. Also the connective tissue shrinks (even the tough dura) much more than the white matter. If a short length of cord with dura slashed transversely over one half and left without transverse cuts over the other half, be placed in bichromate, an hour's time is enough to curve it strongly over toward the side of the unslashed dura.

'Cavities which are ante-facts are, I am convinced from what I saw at that time, due to unequal shrinkage of grey matter and connective tissue on the one hand and of white matter on the other, resulting in rending and cleavage. The cavity in your preparation gives me, on detailed examination, the impression that it has extended to the surface in the hardening. I am led to think there was no fissure which reached the cord in the fresh state, but that in the depth of the posterior horn, or posterior part of grey matter further forward, there was either an actual cavity or a region of altered, loosened, atrophic tissue which, under hardening and dehydration, shrank greatly, splitting as it did so the weakest part of the wall of tissue adjoining. I imagine this happened when in the bichromate and before the preparation was placed in spirit, because the tissue bounding the cavity and cleft bear marks of having been particularly under the action of bichromate.

'Your letter does not mention what muscular groups were involved. Of the preparations received, none seem lower than the 2nd sacral segment, none higher than the 4th lumbar. The anterior horn cells therefore are those innervating, in segmental series downward, the pretibial muscles and dorsal of foot, the post-tibial muscles, the hamstring muscles, the soleo-gastromanius and plantars. I presume that at least some of those suffered as in the usual form of the disease. I am the more impressed therefore by not being able to detect any indubitable departure from the normal in the cells of either anterior horn in any of the preparations; they appear normal in size, number and grouping.

'There is, it is true, some asymmetry, but not more than is commonly met with—perhaps because it is very hard to keep the plane of a section mathematically accurately transverse. The sections are the more instructive as they give good opportunity of examining some of the motor roots. These appear absolutely normal in every instance available.

'The posterior roots are also quite normal in appearance. The groups of very small fibres (not present in the anterior roots of this region) form a normal constituent of the sensory roots of the region, and seem about usual in number and perfectly sound.

'The cells *close* outside the lateral edge of the posterior cornu are well seen, but *not unusually* numerous. Belonging to the group is the one with the long, so far as seen unbranched, process directed toward the place of entrance of the posterior root. I cannot think the process does get *into* the root: it is probably one which turns up or down in the lateral white column. The

cell reminds one, but it would not be possible to state positively that it be so, of one of Cajal's "phoricordonal" cells lying near the posterior cornu and giving *two* axis cylinder process, one to the lateral column and one to the posterior column. (The same cell seems visible in the two sections.)

'The carmine stained islets no larger than ganglion cells which lie further out from the lateral tip of the posterior horn do not appear to me to be nerve-cells: one has a capillary (in cross section) bedded in it, another had a tiny neuroglia cell in it, none have any nucleus like the nucleus of a ganglion cell. These little islets are I think outlying bits of the gelatinosa of the posterior horn. I have never noticed such before, but I am strongly of opinion that is what they are.

'The growing up, and epithelial proliferation, about the central canal is of course common enough in the cords of persons over forty, but is rare in my experience at ages earlier than that.'

In answer to a further letter, Professor Sherrington adds:—

'I did not refer to the cells in the posterior column between Clarke's column and the posterior median fissure, and am sorry I omitted to do so. They are a normal feature of the cord, especially I think of the human cord, in which Clarke's column is better developed than in any animal. No mention of the cells is, so far as I know, made in any book; for that reason I wrote a short account of them not long ago, and gave some figures illustrating their position. I think they must be considered outlying members of Clarke's column. I post you with this, a copy of the paper which contains one's reasons for thinking the cells are cells of Clarke's column. A point of interest in your specimen is that they occur in the 4th lumbar segment (if I am not mistaken in judging by the features of the sections), and I have never previously met with the cells lower than the 3rd segment, which itself often contains none, though the 2nd always does

'As to the cells in the lateral column outside the posterior horn, I think them more abundant in your sections than I have ever noticed before; it is, however, quite usual for a section here and there from this region of cord (human) to contain one or two.'

Case V. (Case G in this family.)—J. G., aged 8, was first seen on 17th February 1893. The patient presented all the features of pseudo-hypertrophic paralysis in an early stage.

Previous History.—This patient began to walk when he was eighteen months old. He was always more or less stiff in his movements; he could never run and jump like other boys.

In this case the disease commenced gradually and without any obvious cause, when the patient was four years of age. In his case it was noticed rather earlier than in the other two patients, his mother says because they were on the look-out for it.

Condition on 17th December 1893.—The patient is well nourished, and tall for his age.

The gait is typically waddling; the back hollowed out in the lower dorsal and lumbar regions. The patient gets up from the floor in the characteristic pseudo-hypertrophic manner. When held up by the armpits, the shoulders go up to the ears.

The calves are large, measuring 10 inches. The thighs are somewhat enlarged, measuring 11 inches. The knee-jerks are absent. The bladder and rectum are normal. The sensory functions are normal. The patient is a bright, intelligent boy; the general health is good; there is no visceral disease.

The condition of the patient at this date is represented in Plate LXXXVIII. Fig. 3.

Condition on June 16th, 1894.—The patient was at this date again carefully examined. He was very much worse. The following notes were taken:—

The disease has made rapid progress of late; the patient is now unable to stand or walk. There is marked retraction of each tendo Achillis with drawing up of the heel. The calves are still relatively enlarged, but they have undergone considerable atrophy during the past year. The right calf now measures 9½ inches and the left 9 inches. The right thigh measures 10 and the left 10¼ inches. The infraspinati muscles are slightly enlarged; the pectorals very much wasted; the serratus magnus slightly hypertrophied.

The patient is able to crawl about the floor, but the arms are so weak that they frequently give way. He often tumbles while creeping and bites his lip. At the present time a scar is present on the lower lip, the result of a wound inflicted in this manner.

The general health is quite good.

Condition on 9th October 1896.—During the past two years the patient has been confined to bed. The general heath has been quite good; the intellectual faculties bright; but the muscular weakness has steadily increased. So far as his lower extremities are concerned he is now a helpless cripple and the upper extremities are very feeble. The lower extremities are the seat of marked contractures (ankles and knees). The muscles both of the lower and upper extremities are greatly emaciated; the muscular wasting is more marked in the thighs and arms than in the legs and forearms; the infraspinati appear to be still slightly enlarged; parts of the calf muscles and trapezii also present some (slight) signs of pseudo-hypertrophy. The facial muscles and the tongue do not appear to be affected.

No fibrillary twitchings were observed.

The knee-jerks are absent.

The bladder and rectum are normal.

The sensory functions and the intellectual faculties are absolutely normal.

The viscera are all healthy.

From the following table of measurements it will be seen that the limbs have grown considerably in length, but have diminished in thickness. The feet have grown but the hands and fingers are small; the patient's mother volunteered the remark that 'the hands have not grown at all.'

Measurements.—The detailed measurements are as follows:—

	Feb. 1893. Inches.	1894. Inches.	Oct. 1896. Inches.
Length of thigh		13¼	14½
„ fibula		11	12½
Thickness of thigh, thickest part	11	10¼	9½
„ „ calf „	10	9	8½
Length of humerus			10
„ ulna			7¾
Thickness of arm, thickest part			6
„ „ just below the tendon of the deltoid			5½
Thickness of forearm			6½
Length of hand, wrist to tip of middle finger			5
Length of middle finger			3
„ foot			8

The four female children in the family all remain unaffected; they are tall and well-developed girls.

Remarks.—In these three cases the disease seems to have commenced at much the same age—about the fourth or fifth year; in all of them the disease advanced slowly until the tenth year, when the power of walking and standing was rapidly lost. In the two elder patients extreme muscular atrophy was developed after this date; both patients died at the age of 18 from an intercurrent complication (bronchitis and pneumonia). In the third brother the disease is pursuing exactly the same course.

In the second case in this family (Case IV.) the muscular atrophy was so extreme that when I first saw this patient I was inclined to doubt whether it was really a case of pseudo-hypertrophic paralysis. The muscular atrophy was so extreme as to suggest a lesion of the anterior horn of the spinal cord (poliomyelitis anterior acuta) rather than of pseudo-hypertrophic paralysis. But (a) the history of the case (the way in which the disease had developed, the condition of the muscles, the character of the gait in the early stages as described by the patient's mother); and (b) the condition of the patient's younger brother—for in his case the typical characteristics of pseudo-hypertrophic paralysis were all present—proved without any doubt that the case was actually one of pseudo-hypertrophic paralysis. And this opinion was confirmed by the condition of the muscles post mortem. The changes in the muscles (see Dr. Muir's report) were quite typical and characteristic (see Figs. 3 and 4, Plate XC.). The multipolar nerve cells in the spinal cord were numerous and healthy, and the peripheral nerves were normal.

It is interesting to compare this case with a case figured by Hammond in his work on the Nervous System (see Fig. 61, p. 538). I must confess when I first saw that plate I doubted the correctness of the diagnosis, and I may say that when I showed the photographs of my own patient to Dr. Marinesco during his recent visit to Edinburgh, he at once expressed doubt as to the case being one of pseudo-hypertrophic paralysis.

It is important to note *firstly*, that in the second brother the growth of the bones (in length) was not interfered with; and *secondly*, that notwithstanding the extreme degree of muscular atrophy which had been present for several years before the

patient's death, the multipolar nerve cells in the anterior cornua of the spinal cord were (with the exception of a very slight fatty and pigmentary change in a few isolated cells) perfectly normal in every respect. Indeed one could not wish to see a more perfect demonstration of multipolar nerve cells than in Dr. Muir's beautifully prepared sections of the lumbar enlargement of the spinal cord in this remarkable case of myopathic muscular atrophy, supervening upon typical pseudo-hypertrophic paralysis.

The series of cases is then specially interesting because of the extraordinary degree of muscular atrophy which has been ultimately developed, and because of the fact that the case of the youngest patient has been carefully watched for the past three and a half years—from the pseudo-hypertrophic stage to the stage of muscular atrophy and contracture. No doubt, if this patient survives for a few years, his condition will ultimately be identical with that of his elder brother. (See Plate LXXXVIII. Figs. 1 and 2.)

Case VI. Typical pseudo-hypertrophic paralysis.

J. H., aged 11, was seen at the Royal Infirmary on March 18th, 1894, suffering from an advanced stage of pseudo-hypertrophic paralysis.

Previous History.—The patient's father states that the difficulty in walking began two years ago, but the disease was evidently in existence before this, for the boy used frequently to fall before the feebleness in walking was recognised as the result of disease. The onset was gradual and without any obvious cause. The patient's general health has always been good. He was three years old before he walked. When the disease commenced he used to walk on his toes.

Family History.—The parents are healthy people. No similar case has, so far as is known, occurred in any of their relatives.

The family consists of six children, three boys and three girls. The patient is the only member of the family who is, so far, affected. The ages of the children are as follows:—

A. Boy, aged 15; quite well.
B. Girl, aged 13; „ „
C. *Patient*, boy, aged 11; *affected.*
D. Girl, aged 6; quite well.
E. Boy, aged 3; „ „
F. Girl, aged $\frac{7}{12}$; „ „

Condition on March 18th, 1894.—The patient is now quite unable to stand or walk; indeed, he is so feeble that he cannot turn over from his back on to his face.

The calves, thighs, buttocks and infraspinati muscles are enlarged and firm. The right thigh at its thickest part measures 12, and the left $12\frac{1}{8}$ inches. The right calf measures $8\frac{3}{4}$ and the left $9\frac{1}{8}$ inches.

The pectoral muscles and muscles of the upper arm are atrophied. The deltoids are slightly enlarged. The facial and tongue muscles are natural.

There are no fibrillary twitchings. The patient was only seen once and the electrical reactions were not tested.

The plantar reflexes and the knee-jerks are absent. The cremasteric reflex is present on the left side. There is no testicle on the right side of the scrotum.

The bladder and rectal reflexes are normal.

The sensory functions are quite natural.

The intellectual faculties are normal.

The appetite and general health are excellent. There is no visceral disease.

Subsequent History.—I have not had the opportunity of seeing this patient again, but Dr. Lorraine, who kindly sent him to the hospital, tells me (October 15th, 1896) that 'he remains very much *in statu quo*; he has, however, got very stout (in this respect the case forms a very remarkable contrast to Cases III., IV. and V.); as he sits in his chair he looks very well, even intelligent; appetite good; sleeps well; is very anxious to have something done for him.'

Case VII. Pseudo-hypertrophic paralysis with marked muscular atrophy.

T. S., aged 12, was seen at the Edinburgh Royal Infirmary on 21st June 1890, suffering from marked muscular atrophy, the result of pseudo-hypertrophic paralysis.

Previous History.—The difficulty in walking was first noticed four years ago when the patient was eight years old. Difficulty in going downstairs was the first symptom; he had to place one leg before the other in order to get down. His father states that at that time his legs were 'terribly thick' in the calves, but that 'now they are getting smaller than they were in the "bran".' The disease commenced gradually and without any obvious cause. As a child, the patient used to suffer from bronchitis.

Family History.—The patient is the eldest of four children; his two brothers and his sister were, when the patient came under my notice, unaffected. One of the younger boys has since manifested symptoms of the disease, but I have unfortunately not had an opportunity of seeing him.

Present Condition.—When the patient stands erect, there is a deep hollow in the back due to antero-posterior curvature in the lower dorsal and lumbar regions; the shoulders are thrown back, but a line let fall from the scapula falls within the pelvis. (See Figs. 4 and 5, Plate LXXXVIII.)

The gait is very peculiar; the patient walks with a very loose gait; this and the atrophied condition of the limbs reminds me of a spider crab.

The calves are relatively large and firm; the muscular power of the calf muscles appears to be good, for the patient can raise himself well on his tiptoes. The left calf measures $10\frac{1}{2}$ and the right $10\frac{1}{2}$ inches. The thigh muscles are markedly atrophied. The left thigh measures at its thickest part $10\frac{3}{4}$ inches and the right $10\frac{1}{4}$ inches.

The buttocks are not enlarged.

The infraspinati, pectorals, muscles of the shoulder girdles and upper extremities including the deltoids are markedly atrophied.

The knee-jerks are absent; the plantar reflexes natural; the cremasteric reflexes very lively. The organic reflexes are normal.

The patient gets up from the ground in a characteristic pseudo-hypertrophic manner; but before he climbs up his thighs he places his legs very widely apart (see Fig. 11, p. 86). It is extraordinary that he can raise himself in this way to the erect position.

There is some talipes equinus, and the foot is shaped very much like that of Friedreich's ataxia. The tendons on the front of the foot are prominent.

There is some vasomotor mottling of the legs and feet.

The sensibility of the skin is normal. There is some doubt as to the condition of the muscular sense, for the patient cannot find his toe when his eyes are shut and it is held up in the air. The power of appreciating weights tied on to the foot seems normal.

Co-ordination is perfect.

The patient is a very sharp boy; his father says that the schoolmaster is very much put about at his being away from school.

The general health is excellent. The thyroid is slightly enlarged.

Treatment.—Arsenic, strychnine, iron, cod-liver oil, massage and faradism were in turn prescribed.

Progress.—The patient gradually got worse, and died in December 1893. There was, unfortunately, no post-mortem examination.

Remarks.—When this case came under my notice it resembled the juvenile form of the disease, rather than pseudo-hypertrophic paralysis; but in the earlier stages of the case the calf muscles had been greatly enlarged. The case was clearly, therefore, one of pseudo-hypertrophic paralysis with a very marked degree of muscular atrophy.

Case VIII. The facio-scapulo-humeral type of Landouzy and Déjerine: Death from influenza and bronchitis: Post-mortem examination: Very little change in the affected muscles.

G. J. A., aged 10, was sent to me on November 13th, 1892, by the late Dr. Chapman of Inverness, complaining of muscular weakness and difficulty in walking.

Previous History.—At the end of December 1891, the patient had a mild attack of influenza; he was not laid up with it. The difficulty in walking was first noticed after the influenza, and has gradually increased since. His father says that he is so weak on his legs that the slightest push is sufficient to shove him over; his legs are apt to double up under him, especially when he goes up or down a hill; he is consequently apt to fall. He has great difficulty in going up and down stairs and in raising his foot over any obstacle. He is gradually getting worse. His parents have been obliged to take him from school, for they were afraid he would fall going up and down the hill on which their house is situated.

Before this disease commenced, the patient enjoyed good health. He had a slight attack of measles when eight years of age. He used to have nightmare, but has not been troubled in this way for a long time.

Family History.—The patient is the eldest of five (living) children; their ages are as follows:—

A. *The patient*, boy, aged 10¼
B Girl, aged 7; healthy.
C. „ „ 6; „
D. Boy, „ 4½; „
E. „ „ 3½; „
F. „ died of influenza when 11 months old.

The parents are healthy people. The near relatives on both sides of the house are very healthy and robust. No case of a similar kind has ever occurred in any of the patient's relations.

Present Condition.—(November 13th, 1892) The patient is a tall, healthy-looking boy. The general health is excellent. Intellectually the patient is bright, sharp, and full of fun. He is a splendid sleeper.

The gait is waddling. In the erect position, the spine is curved in the antero-posterior direction, the shoulders thrown backwards and the chest forwards.

The calves feel hard and firm; in comparison to the thighs they are relatively somewhat large; none of the other muscles are enlarged. The pectoral and scapular muscles and the muscles of the upper arms are markedly atrophied.

The right calf measures 10 and the left 10 inches. The right thigh measures 11½ and the left 11½ inches. The right forearm measures 7 and the left 6¼ inches. The right arm measures 6¼ and the left 6⅛ inches.

The feet are large and flat, and the hands are large.

Very distinct fibrillary twitchings are to be observed in the muscles of the back, in the pectorals and muscles of the upper arms.

The muscles contract briskly to the faradic current; there is no reaction of degeneration.

The knee-jerks are active. The plantar reflexes are brisk. There is no affection of the bladder or rectum.

The sensory functions are quite normal. There is no vasomotor mottling of the skin.

The circulatory, respiratory, alimentary and urinary systems are normal.

The condition on 22nd December 1894.—The patient was seen with Dr. Forsyth at Inverness on 22nd December 1894, and was admitted to the Edinburgh Royal Infirmary on 14th January 1895. The following notes were made on 22nd December 1894, and the observations subsequently checked while the patient was in the Infirmary.

During the two years which have elapsed since I last had the opportunity of examining the patient, the disease has steadily progressed in a downward direction. The patient is now unable to stand or walk unless supported. He has grown greatly in height and now looks both old and big for his years. The sexual development is precocious; the pubes are covered with hair and the penis and testicles are much larger than in the average boy of his age.

The muscles of the calves do not now appear to be enlarged; the muscles of the thighs are somewhat enlarged; the buttocks are of normal size. The muscles of the back are atrophied. The scapular muscles (including the infraspinati), the pectorals, the latissimi dorsi, the lower portions of the trapezii and the muscles of the upper arm are extremely wasted. The deltoids, particularly the left deltoid, are slightly but distinctly enlarged. The forearms are rounded, the muscles distinctly atrophied, though much less so than those of the upper arms. The small muscles of the hand are affected; the hands are weak and there is a distinct commencing bird-claw condition; the thenar and hypothenar eminences are wasted. The hands and feet are cold to the touch and of a purple colour; but the patient says he does not feel cold; indeed, he enjoys being out even in cold weather.

The *measurements* at this date were as follows (I append the measurements on November 13th, 1892, for comparison):—

	Dec. 22, 1894. Inches.	Nov. 13, 1892. Inches.
Right calf, at thickest part	9⅞	10
Left calf „ „	9⅞	10
Length of foot from heel to tip of big toe	9	
Right thigh at thickest part	14	11½
Left „ „ „	13¾	11½
Right upper arm at thickest part	7½	6⅜
Left „ „ „	7½	6¾
Right forearm at thickest part	7¼	7
Left „ „ „	7	6¼

Occasional fibrillary twitchings were observed in the pectoral, but not in any of the other, muscles.

On attempting to raise the patient by the arm-pits, the shoulders go up to the ears.

The knee-jerks are absent; they were present in November 1892.

The functions of the bladder and rectum are unaffected.

The condition of the face.—The facial muscles appear to be more markedly involved than any of the other muscles. When I saw the patient two years ago I was suspicious that there was some involvement of the muscles about the mouth, and I wrote to Dr. Forsyth some time after I had first seen the patient, asking him if he could send me a photograph of the boy's face, in order that I might study this point more carefully.

On 22nd December 1894, the patient's mother, who is very intelligent, told me that the first defect which she had noticed was a difficulty in smiling and moving the lips; this was apparent before the difficulty in walking was observed.

The patient's expression is peculiar. His face and head are large; the head is covered with a great profusion of thick coarse black hair. The expression is sedate and stolid-looking. The face is pale; about the eyelids it looks full and slightly swollen. The lower lip is rather thick and somewhat pouting. The patient cannot close the lips firmly. When asked if he could whistle, his mother answered for him 'He can only whistle through his teeth.' When told to try and whistle, the mouth remained open, the lips were not approximated. As his mother says, he whistles through his teeth. He is quite unable to raise his upper lip so as to show his top teeth. When he smiles, his mouth is drawn out transversely. His mother mentioned this of her own accord (she evidently was a very acute observer). On another occasion, when asked if he could smile, he said, 'No, I look as if I were going to cry when I try to smile.' His friends had, he said, told him this. The muscular power of the cheek muscles is markedly impaired; he is quite unable to suck in the cheek against resistance. The patient can close his eyes, but the power of the orbicularis palpebrarum is notably impaired. When the eyes are closed, slight upward pressure of the finger is sufficient to raise the lids. He cannot wrinkle the forehead. When he is eating, food collects in the sides of the cheeks. The tongue is perhaps slightly enlarged.

Microscopical examination of a portion of the calf muscles removed during life.—During the patient's stay in hospital a small portion of the calf muscle was, with the consent of the patient and his parents, removed under chloroform by Mr. Cotterill. The wound healed by first intention.

The portion of muscular tissue was, immediately after its removal, placed in Müller's fluid. Dr. Muir kindly made sections of it and reported to me as follows:—

'I can find really very little change in this muscle. The fibres on transverse section are more circular, i.e. less polygonal, and are less closely opposed to one another, than in normal muscle, and a few show slight traces of vacuolation, but this is not at all marked. The fibres are regular in size; and on the whole slightly larger than normal; there is no nuclear proliferation nor splitting of fibres, and no lipomatosis.'

Death from pneumonia.—On 10th March 1895, the patient was unfortunately attacked by influenza and pneumonia and died on March 14th, 1895.

Post-mortem examination and report of the microscopical condition of the muscles, spinal cord and peripheral nerves.—The post-mortem examination was made on 15th March by Dr. Leith, to whom my sincere thanks are due for the exhaustive examination which he has kindly made of the tissues and organs, and for the very great time and attention which he has expended on the research.

Muscles.—Portions of the following muscles were examined microscopically:—The buccinator, lip muscles, temporal muscle, splenius, pectorals, infraspinatus, deltoid, biceps, calf muscles, quadratus femoris and gluteus maximus.

NOTE.—In December 1894, the patient was much bigger and his bones much larger than in November 1892. This must be taken into account in estimating the comparative measurements at the two dates. The most striking alteration in the measurements is that while the calves have decreased, the thighs have greatly increased.

The lip, buccinator and calf muscles were the only muscles in which any definite microscopical changes were observed. The other muscles enumerated above were all in a condition of extreme atrophy, but their structure was apparently healthy, the only change noticed being that the muscular fibres were, on transverse section, found to be more circular than normal.

In the lip, calf and buccinator muscles, the muscular fibres, on transverse section, were found to be more circular than normal.

There was no lipomatosis. In some of the muscles, the calf muscles especially, there seemed to be a slight excess of fine fibrous tissue between the muscular fibres.

On longitudinal section many of the muscular fibres appeared to be in a process of longitudinal splitting into smaller fibres. This change was in places apparently preceded by proliferation of the muscle nuclei.

Many of the muscular fibres in these (lip, buccinator and calf) muscles were smaller than normal. This was perhaps the most striking change observed.

A few of the fibres appeared to be hypertrophied, but this change was doubtful.

Spinal cord.—The spinal cord, especially in the cervical enlargement, was distinctly thicker than normal.[1] The structure of the spinal cord was quite normal, except perhaps in the lower part of the cervical enlargement, where some of the fibres of the posterior columns appeared to be arranged in a peculiar whorled manner. The multipolar nerve cells of the anterior horn were numerous and apparently quite healthy.

Peripheral nerves.—The sciatic and posterior tibial nerves were quite healthy.

The small nerves seen amidst the muscular fibres, in transverse microscopical sections, appeared to be quite normal.

Remarks.—In this case, the clinical features when the patient was first seen were those of progressive muscular dystrophy. There was no pseudo-hypertrophy except perhaps in the calves, which were relatively slightly enlarged in comparison with the thighs. The muscular atrophy in the arms and scapular muscles was much more marked than it usually is in the early stages of pseudo-hypertrophic paralysis.

The case is of great interest because of:—(1) The very definite presence of fibrillary twitchings; (2) The active condition of the knee-jerks; and (3) The very slight changes which were found on microscopical examination.

In the portion of calf muscle removed during life, the only apparent change was the uniformly circular shape which the muscular fibres presented in transverse sections.

In the numerous muscles examined by Dr. Leith after death, there appeared to be no microscopical change except the more or less uniformly circular outline of the fibres in transverse section (the same condition which was found by Dr. Muir in a portion of the calf muscle removed during life).

In the lip, buccinator and especially the calf muscles, more decided alterations were present. Many of the muscular fibres were smaller than normal and a few appear to be hypertrophied. Some of the fibres were obviously undergoing longitudinal splitting. In the calf muscles a slight excess of fibrous tissue was present between the muscular fibres.

Considering the extremely atrophied condition of the muscles, the absence of any striking change on microscopic examination is very remarkable, especially when it is remembered that the spinal cord and peripheral nerves appeared to be quite healthy.

When the case came under observation for the second time (December 1894), it was even more interesting and important than it was in November 1892. The condition of the patient in January 1895, and the way in which the case had progressed showed that the diagnosis (progressive muscular dystrophy) which was made when the patient was first seen was correct.

The case seems to form an intermediate link between Erb's juvenile form of progressive muscular dystrophy and the facio-scapulo-humeral type of Landouzy and Déjerine.

If the mother's observation is to be trusted, the facial muscles were involved quite early in the case; possibly they were the first muscles to be affected, but with regard to this I cannot speak definitely. The disease seems to have commenced when the patient was about nine years of age—considerably later than in most of the cases which Landouzy and Déjerine have described.

In December 1894, the case seemed to be a typical mixture of Erb's juvenile form and the Landouzy-Déjerine form of the disease. The affection of the facial muscles was at this date most marked, and the condition of the upper extremities was typical of Erb's juvenile form—atrophy of the scapular muscles, enlargement of the deltoids and atrophy of the upper arm muscles, the forearm muscles being comparatively well preserved. It differs from Erb's juvenile form in its typical stage inasmuch as the small muscles of the hand are distinctly affected and the forearm muscles are beginning to waste. But it must be remembered that in the advanced stages of Erb's juvenile form of progressive muscular atrophy these muscles may be affected.

Landouzy and Déjerine originally believed that the form of muscular dystrophy which goes by their name was a separate and definite disease and that it was not a mere variety; they further thought that in it pseudo-hypertrophy does not occur. This opinion is now abandoned and this case conclusively shows that it was incorrect. In the earlier stages of this case, the calf muscles were relatively enlarged, and at the present time, when the great majority of the muscles throughout the body are markedly atrophied and when the condition of the facial muscles is typical and characteristic, the muscles of the thigh and the deltoids are distinctly enlarged—in a condition of pseudo-hypertrophy.

The existence of distinct fibrillary twitchings was in this case undoubted.

For all of these reasons the case is a most important and interesting one. In passing, I may also allude to the precocious sexual development. I have noted the same thing in more than one other case of progressive muscular dystrophy.

Up to the present time, none of the other members of this family are affected.

[1] I have noted the same condition in another case (the case represented in Plate LXXXVI. Fig. 1); in it the spinal cord was malformed.

Cases IX. and X. Ill-developed pseudo-hypertrophic paralysis or the juvenile form of progressive muscular dystrophy.

The two following cases were sent to me by Dr. Proudfoot of Kirkcaldy on 17th December 1892. They seemed to stand midway between the ordinary form of pseudo-hypertrophic paralysis and Erb's juvenile form of the disease.

Family History.—The patients are brothers. They belong to a family of nine children, one of whom died in infancy at the age of five months, it is said from teething. One of the girls is so demented that she is confined in an asylum. Of the surviving eight members of the family, three girls and two boys are perfectly healthy. The ages are as follows:—

A. Girl, aged 23; small for her age. For the past two years she has been confined to Springfield Asylum. Before that date she was in Roslin Castle. She suffers from dementia which seems to have developed after an attack of 'brain fever' at the age of 14. The details of the case are given below.

B. Girl, aged 21; very strong and healthy, and very sharp mentally.

C. Infant; died at the age of five months from teething.

D. Boy, aged 20; a lithographer; very healthy and strong, and mentally very sharp.

E. Boy, aged 17; a confectioner; very healthy and strong; 'awful' smart' mentally.

F. *Boy* (John), aged 16; *affected.*

G. *Boy* (William), aged 14; *affected.*

H. Girl, aged 10; perfectly healthy and bright mentally.

I. Girl, aged 7; perfectly healthy and very sharp mentally.

So far as it is known, no other cases of a similar kind have occurred amongst any of the patients' relatives.

The more detailed notes of the cases are as follows:—

Case IX.—J. K., aged 16, was first seen at the Edinburgh Royal Infirmary on 17th December 1892.

He is a heavy stupid-looking boy and is mentally somewhat defective.

Previous History.—The disease in his case seems to have commenced in early childhood. He began to walk at the age of eighteen months; he could never run and jump like a healthy boy; and he has always had difficulty in going upstairs; he has always walked with his back very much curved.

From early childhood he has always suffered, and he still continues to suffer, from nocturnal incontinence of urine. His bowels are very readily disordered; porridge and soup bring on an attack of diarrhœa.

Present Condition (*December 17th*, 1892).—He is tall for his age. When standing in the erect position, a very marked hollowing of the back in the lower dorsal and lumber regions is apparent; the shoulders are thrown back and the chest forward (see Plate

LXXXVII. Fig. 6). The gait is slightly waddling and loose-strung.

The calf muscles are relatively enlarged. The thighs and buttocks are of normal size; the muscles of the back very markedly atrophied; the scapular muscles are atrophied; the deltoids slightly enlarged; the muscles of the upper arm markedly atrophied; those of the forearms and hands are natural

The face does not appear to be affected.

There are no fibrillary twitchings. The electrical reactions are normal.

A very slight knee-jerk can be elicited in each leg. The plantar reflexes are present.

Sensibility is normal.

The mental faculties are decidedly below par.

He has difficulty in fixing with the eyes. This is apparently a mental rather than an ocular defect. The ocular apparatus seems to be normal.

The genital organs are well developed; in fact, largely so for the boy's age.

The general health is good; and there is no visceral disease.

Treatment.—Arsenic and strychnine were prescribed and were continued at intervals until November 24th, 1894, when one five-grain tabloid of thymus gland was prescribed three times daily

Subsequent Progress.—Between December 1892 and November 1894, the patient was seen on several occasions at the Infirmary. During this period he slightly improved, and in the spring of 1894 was able to take a situation as an assistant in a confectioner's shop. His aunt, with whom he lives, states that he is undoubtedly somewhat stronger and better.

When examined on *November 24th*, 1894, his condition was practically the same as in December 1892. The calf muscles seemed to be still further enlarged, and felt firm and resistant. A slight knee-jerk could still be elicited in each leg.

The nocturnal incontinence of urine still continues

October 17th, 1896. The patient was seen at the Edinburgh Royal Infirmary to-day and carefully examined.

His aunt with whom he lives says that he has been very well during the past two years, and regularly at work in a baker's shop; he is the youngest apprentice and has to do a good deal of walking about. The only thing that she notices wrong with him is that his hands get very blue when exposed The nocturnal incontinence of urine is much less troublesome. If he is made to get up once through the night he does not now wet the bed.

The gait presents the same characters as before (see note December 17, 1892); the back is still very markedly curved. The calves are still markedly large and firm; the triceps on each side is in places distinctly enlarged (pseudo-hypertrophied), but in other places atrophied. The pectorals, the adductors of the thigh and the biceps in the upper arm are markedly atrophied.

The patient gets up from the ground in the pseudo-hypertrophic manner, but this is not so marked as in his brother's case

The tongue is very large and broad.

The knee-jerks are now completely absent.

The feet and hands are large and the development of the bony skeleton is evidently unaffected.

The genital organs are fully developed.

Measurements.—The following measurements were made:—

	Inches.
Right calf, thickest part	14
Left „ „	14¼
Right thigh, middle	15
Left „ „	15¼
Right arm „	8⅛
Left „ „	8¼
Right forearm, thickest part	9⅛
Left „ „ „	9¼

Case X.—W. K., aged 14, was first seen at the Edinburgh Royal Infirmary on 17th December 1892.

Previous History.—In this case the disease commenced five years ago when the patient was nine years of age. As a little boy he could run and jump like other children. The onset was gradual and without any apparent cause.

Present Condition.—The patient is tall for his age. He is not so heavy and stupid-looking as his brother, but his mental condition is much more impaired. His aunt, who brought him to the hospital, stated that although he has been at school all his life he has practically made little or no progress, and yet in some respects he seems sharp enough, for he brings home all the news of the town and he seems to take an interest in things that are going on round them.

He can hardly read, write, or spell at all. When asked to write 'dog' on the blackboard he wrote 'd g o,' and when asked to write 'cat' he wrote 'c d.' He said that three times six were twelve and three times four were six.

The patient has great difficulty in fixing an object with the eyes. This was well seen when he was examined with the ophthalmoscope. The pupils are equal and react to light. The optic discs are normal. There is no nystagmus.

On stripping him, the calves were seen to be considerably enlarged, decidedly so in proportion to the thighs and buttocks and atrophied upper extremities. The back is markedly curved in the lower dorsal and lumbar regions (see Plate LXXXVII. Fig. 5).

He walks with a characteristic pseudo-hypertrophic gait He gets up from the floor in a typical manner, climbing up his thighs.

When raised by the armpits, the shoulders go up to the ears.

The knee-jerks are completely absent. The plantar reflexes are also absent

The functions of the bladder and rectum are normal.

The genital organs are well developed; in fact, largely so for the boy's age

The sensory functions are normal.

The condition of the muscles.—The calf muscles are considerably enlarged, firm and hard. The thighs and buttocks are of normal size. The deltoids, especially the left, are somewhat enlarged. The infraspinati are slightly enlarged. The scapular muscles are atrophied The muscles of the upper arm are considerably atrophied. The muscles of the forearm and hands are normal.

Treatment.—The patient, like his brother, was treated with arsenic and strychnine.

Subsequent Progress.—On *November 24th*, 1894, his condition was practically unchanged. The calf muscles were rather larger than they were two years previously, the scapular and upper arm muscles more emaciated The pectoral muscles were very markedly atrophied There were no fibrillary twitchings.

October 17th, 1896. The patient was seen at the Edinburgh Royal Infirmary to-day and carefully examined.

His aunt says that during the past two years his general health has been excellent, but the walking is rather worse; he frequently tumbles; he did so this morning in coming to the hospital. He is employed at light work (sitting) in a confectioner's shop. He has great difficulty in going up stairs.

The gait is partly waddling, partly high-stepping. The back is markedly curved.

The heels are slightly drawn up from retraction of the calf muscles.

The calves are large and hard; the thighs markedly atrophied; the buttocks extremely atrophied, indeed all the muscular tissue in the glutei muscles seems to have disappeared.

The long head of the triceps, especially in the left arm, is distinctly enlarged; the other muscles of the upper arm and of the shoulder girdle and scapulæ are atrophied, especially the pectoral muscles. The forearms are well preserved.

The patient gets up from the ground in the typical pseudo-hypertrophic manner (climbing up his thighs).

The knee-jerks are absent.

The genital organs are largely developed.

The hands and feet are large.

The tongue is not enlarged.

Measurements.—The following are the detailed measurements:—

	Inches.
Right calf, thickest part	13¼
Left „ „ „	13¼
Right thigh, middle	12¾
Left „ „	12½
Right forearm, thickest part	8½
Left „ „ „	9
Right arm, middle	7
Left „ „	8½

Note on the sister's case (dementia).—I am indebted to Dr. Turnbull of the Fife and Kinross County Asylum for a detailed account of the case of the eldest sister of the two cases of pseudo-hypertrophic paralysis which have just been related. She is at present in a condition of marked dementia.

Dr. Turnbull's report is as follows:—

'Catherine K. Twice admitted to Fife District Asylum; first admission was on Jan. 30th, 1888, and at that time the following notes of her case were taken:—Age 21; single; assists at home in housework; brought from 165 Roslyn Street, Gallatown, Kirkcaldy.

'**Previous History.**—Natural disposition bright and cheerful; bashful. As a child was very intelligent until in 1881, aged 14, she had an illness which her father describes as brain fever. This lasted for four months and probably was some form of mental affection, for it was noted that she was never thoroughly well in mind again after the illness. She was duller, different from her usual self and very irritable in temper. In 1884, she suffered from an attack of acute mania, was sent to Rosewell Asylum and was there for a year. She was sent home in November 1885 much quieter in conduct, but regarded as being only improved, not fully recovered. After this she made herself useful in the house in a kind of way, but would brook no interference, was very short tempered and was sometimes very irritable with the other children. In the end of 1887 she got excited again, took to wandering out of the house at all hours, was violent to those around her, and consequently had to be sent to the Asylum here on January 30th, 1888.

'Previous insanity in family denied.

'Patient began to menstruate in 1881 about the time that the mental symptoms first showed themselves.

'**State on Admission, Jan. 30th, 1888**:—Mentally dull, stupid, would not speak; evidently enfeebled but showing no definite delusion and quiet in conduct. Bodily health average, showing no special derangement of any kind; and sensory and motor functions appearing normal.

'**Progress.**—While in the Asylum, she brightened up considerably, would answer questions and do work, but was still silly in manner and childish in conversation; gained in bodily health; weight increased, and menstruated regularly. On September 29th, 1888, she was discharged relieved, and sent home showing still mild enfeeblement of mind, without delusions and being quiet in conduct and manageable.

'For fully 12 months after going home she got on very well, was contented, docile, and made herself useful in housework; but in the end of 1889 she again got unsettled, being discontented, irritable, quarrelsome, expressing delusions about being poisoned, about being killed and put through a wall, etc. She got steadily worse, became violent, assaulting her father, etc., occasionally threatening to drown herself, and so troublesome that ultimately she had to be sent back to the Asylum on Feb. 4th, 1890.

'**State on Admission, Feb 4th, 1890**.—Mentally marked enfeeblement with considerable excitement, chattering a lot of incoherent nonsense, laughing to herself and very silly in her general conduct.

'Bodily condition was not so good as when she left the Asylum, but there was no special bodily ailment, and motor and sensory functions were normal.

'**Progress.**—For a time had distinct bursts of excitement, but of late these have become less marked and she is now much more easily managed, but has at the same time become markedly more enfeebled in mind, and now needs much attention from her nurse to keep her correct in her habits, etc.

'In its clinical aspect the case is one of insanity coming on at the period of puberty, due probably to hereditary predisposition (though this is denied in the history), becoming aggravated during the adolescent period, and (in place of recovery) passing into confirmed chronic dementia.

'**Condition on 15th October 1894**:—Age 27. Ht. 5 ft. 3 in. Wt. 8 st. 4 lbs.

'Patient is rather a silly-looking girl, and if she sees any one taking notice of her goes off into a giggle and continues giggling for some time. She is very taciturn and can only be made to reply to questions with considerable difficulty. She is now very demented, and this along with the taciturnity makes it very difficult to know exactly how she feels and what she feels. She takes her food fairly well and sleeps well: she does a little housework, such as brushing the Ward floor, etc. She walks with a slight stoop, but otherwise her gait has nothing remarkable in it.

'*Respiratory System.*—Normal.

'*Circulatory System.*—Pulse 84, regular in time and rhythm and of fair tension and volume. Heart normal in size and sounds are normal.

'*Digestive System.*—Appetite good. Bowels inclined to be constipated. Tongue large and flabby looking. Teeth poor. Liver and spleen are normal in size.

'*Genito-Urinary System.*—Urine, sp gr. 1024. Nothing abnormal in it. Menstruation quite regular.

'*Nervous System.*—Ordinary motor power seems normal. Ordinary sensation seems to be impaired somewhat, but difficult to be quite certain of this. Plantar reflex cannot be elicited. Patellar reflex not well marked, but present. Pupils equal and regular. React both to light and accommodation, but are sluggish.

'*Locomotory System.*—Muscles are rather soft and flabby, more especially in the legs, but they are not increased in size on any part of the body. There is no impairment of co-ordination or balancing power.

'*Mental Condition.*—Marked dementia.'

Cases XI., XII., XIII. and XIV. Cases of pseudo-hypertrophic paralysis and progressive muscular dystrophy.

These cases, which were seen with Drs. Gill and Mason at Langholm on 15th May 1891, were all subsequently admitted to the Edinburgh Royal Infirmary under my care. They are of great interest, for in two of them (the youngest patients) the clinical features of the disease are at present suggestive of the pseudo-hypertrophic type, in the third the condition presents all the characteristic features of myopathic muscular atrophy (extreme muscular atrophy but absolutely no pseudo-hypertrophy); while in the fourth (eldest boy's case) a combination of the two types appears to be present.

Erb's opinion that the different forms of progressive muscular dystrophy are mere varieties of the same disease seems therefore to be confirmed in this family, so far at least as the clinical features are concerned; but the microscopical changes in the muscles of the younger boy do not resemble those characteristic of the advanced stages of pseudo-hypertrophic paralysis.

The elder girl's case is of great scientific interest. In it most marked fibrillary tremors were repeatedly seen by several independent observers in some of the affected muscles. It is peculiar, inasmuch as, although the disease did not commence until she was three years old, it has advanced much more rapidly than in the case of her older brother, in whom it commenced at the age of fourteen months. Further, it was most carefully observed during life and exhaustively examined by Dr. Muir after death. The alterations which the muscular fibres presented on microscopical examination were very striking, and they are all the more interesting since in her two brothers' cases portions of the affected muscles were removed during life, and the microscopic changes in the muscles of three of the affected patients in this family are therefore available for comparison.

The cases are exceptional, inasmuch as none of the ancestors or collaterals are affected.

Family History.—The father is a tall healthy man aged 37; the mother a stout healthy woman aged 36.

So far as is known, no other cases of a similar nature have occurred amongst any of their relatives.

The mother is one of ten children. Several of her brothers and sisters are married and have large families, none of their children (the cousins of these patients) are affected. Her grandparents, father, mother, uncles and aunts were healthy people.

The father has one brother and one sister, both unmarried. His father and mother are still alive and healthy.

The family has consisted of seven children. One died when three months old. The remaining six are all living—two boys and four girls. Both the boys and two of the girls are affected. Their respective ages are as follows:—

A. *Boy*, aged $13\frac{2}{12}$; *affected*. In this case the disease commenced at the age of fourteen months. It presents many of the clinical characters of pseudo-hypertrophic paralysis; but the muscular atrophy in the upper extremities is more marked than in most cases of pseudo-hypertrophic paralysis. (Full notes given below.)

B. *Girl*, aged 11; *affected*. In this case the disease commenced at the age of three years. It presents the characters of progressive muscular dystrophy without pseudo-hypertrophy, for none of the muscles (except perhaps the glutei) are enlarged. (Full notes given below.)

C. Girl, aged 10; unaffected; very strong and healthy. Her parents state that from the time she commenced to run about it was evident that she was quite different from the other children. She could always run and jump freely; none of the others who are affected could do so. She never had any difficulty in going up stairs; all the affected children had great difficulty in going up stairs.

D. *Boy*, aged 8; *affected*. In his case the disease commenced at the age of 6. As yet it is only slight. In this case the disease presented some of the clinical characteristics of commencing pseudo-hypertrophic paralysis, but the microscopical condition of the muscles is quite peculiar and in no way suggestive of this (the pseudo-hypertrophic) type.

E. *Girl*, aged 6; *affected*. In her case the disease commenced at the age of 5. As yet it is only slight; but it looks as if it would assume the same form as the younger brother's case. (Full notes of this case are given below.)

F. Girl who died at the age of three months.

G. Girl, aged 1½; unaffected. She runs with free action like her sister who is unaffected.

The father spontaneously stated that the first alteration in the muscles which he observed was softness and flabbiness of the lower part of the thighs; then, in all of the cases except the eldest girl, the 'bran' (calf) 'of the legs became big.'

The more detailed notes of the cases are as follows:—

Case XI. (A.)—James P., aged 13, was admitted to Ward 27, Royal Infirmary, Edinburgh, on 22nd December 1894, suffering from pseudo-hypertrophic paralysis and myopathic atrophy.

Previous History.—The muscular weakness was first noticed when the patient began to walk at the age of fourteen months. Since then the disease has slowly but gradually progressed. He has never walked well, has never been able to run or jump, and has always had difficulty in going up and down stairs. He began to go to school when he was five years of age and has continued to go to school since. His general health has always been good. Five years ago he had an attack of influenza and was confined to bed for about a week.

State on Admission.—The patient is a tall well-grown boy. His height is 5 ft. ¾ ins.; his weight 7 st. 4 lbs. His only complaint is muscular weakness and difficulty in walking. He states that in going to and from school he often falls, sometimes forwards, sometimes backwards. He has frequently hurt himself somewhat severely. Scars are seen on both knees and in the occipital and left temple regions. The patient says that after falling on the back of the head he has frequently been stunned and always has a headache and is sick afterwards.

The lower limbs as a whole look big and large when contrasted with the upper extremities, which are markedly wasted.

Attitude in the erect position.—When standing in the erect position the back is markedly curved; the upper part of the abdomen is thrown forwards and the shoulders backwards. A plumb line from the middle of the shoulders falls a considerable distance outside the sacrum. There is slight drooping of the left shoulder as compared with the right. The left heel is somewhat drawn up (retraction of the calf muscles).

Gait.—The patient takes fairly long steps and in walking does not waddle and put his feet wide apart like most patients affected with pseudo-hypertrophic paralysis. He is somewhat knock-kneed, so that in walking the knees rub against one another. In walking, the heels are first raised from the ground, the action is high stepping and the back markedly curved.

Mode of rising from the recumbent to the erect position.—He gets up from the floor in the characteristic pseudo-hypertrophic manner, but this mode of rising presents one peculiarity which I have not noticed before: after he has raised himself on to his toes and fingers, he draws his right foot forward with his right hand, then grasps his right thigh with his left hand, then puts his right hand on the top of the left and then raises himself into the erect position. (See Plate LXXXIX. Figs. 1 and 2.)

He has great difficulty in getting into the sitting position when in bed or in rising from a chair; he can only do so by the help of his arms.

Power of fixing the shoulders against resistance.—When the patient is raised by the shoulders, the hands being placed in the armpits, the shoulders go up to the ears.

Condition of the muscles.—There is no definite paralysis. All the movements of the body can be performed, but with little force. The muscles of the upper extremities in particular are very feeble. The facial muscles do not appear to be affected; the patient can whistle.

Lower extremities.—The muscles of the calf are firm and well developed. The muscles on the anterior aspect of the leg appear to be atrophied. The muscles of the thigh are somewhat soft and flabby, the extensors more so than the flexors.

The muscles of the buttock are well developed and apparently somewhat enlarged; the right buttock is larger than the left.

Upper extremities.—The muscles of the upper arm are soft and markedly atrophied. The muscles of the forearm are slightly atrophied. The thenar and hypothenar eminences are flattened. The interossei muscles appear to be somewhat atrophied.

Muscles of the shoulder girdle.—The normal roundness of the shoulders is lost, but some fasciculi of the right deltoid muscle appear to be hypertrophied. The right deltoid is larger than the left, which is markedly atrophied.

The infraspinati are perhaps slightly enlarged, but this is doubtful.

The pectoralis major, serratus magnus, latissimus dorsi, trapezius, rhomboids, and levator anguli scapulæ all appear to be atrophied.

The extensors of the spine appear to be atrophied.

The abdominal muscles feel firm and do not appear to be affected.

As a whole, the extensor muscles seem more affected than the flexors.

The *facial* muscles do not appear to be affected.

The *tongue* is not affected.

The pelvis is very broad and the back and shoulders narrow.

Fibrillary tremors frequently occur in almost all of the atrophied muscles; they are most marked in the trapezius, latissimus dorsi, pectoralis, deltoids and muscles of the upper arm, especially the triceps. In the calves and buttocks the tremors are seldom if ever observed.

Electrical reactions.—All the muscles react to the faradic current, but much less forcibly than in health. The galvanic reactions are normal.

Myalgic pains.—The patient states that he sometimes feels pain in the calf muscles when he gets tired; and he states that when he wakes in the morning his neck is often stiff and sore, and that he has pain in the outer aspect of both legs. This pain disappears after he gets up.

Reflexes.—The plantar reflex is absent; the abdominal and epigastric reflexes are slightly marked; the infrascapular reflex is present; the palmar reflex absent.

The knee-jerks are completely absent.

The visceral reflexes (bladder and rectum) are normal.

Co-ordination is perfect. The patient can walk and stand with his eyes closed, but when in the erect position the muscular weakness is so great that the slightest touch is sufficient to throw him over.

The sensory functions are unimpaired.

Intellectual faculties.—The patient seems to be a bright sharp boy, but he says that his memory is very bad. He states that he has to carry a note-book about with him to record everything which goes on. He appears to be nervous and easily frightened and does not sleep well.

The circulatory, respiratory, digestive and urinary systems are normal. The general health is excellent.

The *temperature* is continuously subnormal.

Measurements.—The detailed measurements were as follows:—

	Inches.
Right arm, thickest part	7½
Left „ „ „	7¼
Right forearm, thickest part	7
Left „ „ „	7
Right thigh, middle	14½
Left „ „	14¼
Right calf, thickest part	12
Left „ „ „	12

On 19*th February* 1895, a portion of the left biceps muscle was removed by Mr. Cotterill (with the consent of the patient and his friends) under chloroform. The wound healed by first intention. The portion of muscle removed was immediately placed in Müller's fluid and handed to Dr. Muir, who kindly made sections of it and reported as follows:—

'**Microscopical condition of a portion of the left biceps removed during life.**—This showed changes of the same nature to those described in the case of Isabella P. (Case XII. p. 107.) There were enlarged fibres, which showed signs of degeneration, irregular swelling, nuclear proliferation, etc. The most striking feature, however, was the presence of fasciculi composed almost entirely of very minute fibres of nearly uniform size and pretty regularly arranged. In the transverse section of one fasciculus, for example, I counted ten

fibres much enlarged and more than one hundred small fibres, there being practically no intermediate forms. (Plate XC. Figs. 5, 6 and 7 shows a portion of this fasciculus.) In some places there was little or no nuclear proliferation around the small fibres, in others proliferation was very marked (Plate XC. Figs. 5 and 6). There was some interstitial increase of fat in this muscle.'

Treatment and Progress of the case.—The patient remained in hospital until March 14th, 1895. He was treated with thymus extract, arsenic, strychnine (hypodermically), massage and the faradic current. He gained strength and at the date of his discharge could walk more freely and rise more easily from the recumbent position.

Case XII. (B.)—Isabella P., aged 11. Height 4 ft. 6¾ ins.; weight 4 st. 10½ lbs. This patient was admitted to Ward 27, Edinburgh Royal Infirmary, on May 26th, 1894.

Previous History.—Nothing was amiss with the patient until she was three years old; her back then seemed to get weak. During infancy she enjoyed good health. She was long in walking.

The disease commenced slowly and gradually and without obvious cause. When three years of age she seemed to be very easily tired with walking. She has never been able to run freely or to jump. Since the disease commenced she has had great difficulty in going up stairs.

The patient had scarlet fever at the age of seven and two attacks of mild influenza at the age of ten. The muscular weakness did not seem to be materially increased after the influenza.

During the past three or four months, the patient seems to have gained a little strength; she is able to play longer at a time and to walk further than she could before.

Present Condition.—The mouth is somewhat pouting. The muscles of the back, scapulæ, shoulder girdles, upper and lower extremities, with the exception of the glutei muscles, are all markedly atrophied.

Attitude in the erect position.—When standing in the erect position the back is curved, the chest and upper part of the abdomen thrown forward and the shoulders backward, but the feet are kept close together and the patient does not stand on her tiptoes. In addition to the marked antero-posterior curve of the lower dorsal and lumbar regions, there seems to be a slight lateral curvature of the spine in the dorsal region, the convexity being to the left. The thorax is flattened from before backwards and there is a marked depression below the lower ribs and zyphoid cartilage in the epigastric and adjacent parts of the hypochondriac regions. (See Plate LXXXVII. Fig. 4.)

Gait.—The gait is not 'waddling'; it is feeble; the patient seems to have great difficulty in flexing the thigh on the abdomen.

The patient is unable to run or jump, and has great difficulty in going up and down stairs.

Mode of rising from the recumbent to the erect posture.—At the time of her admission to hospital she was quite unable to raise herself from the recumbent to the erect position; she could get into a sitting position and that was all. In the course of a month she was able to raise herself to the erect position in the typical pseudo-hypertrophic manner—climbing up her thighs.

Power of fixing the shoulders against resistance.—On attempting to raise the patient by the shoulders, the hands being placed under the armpits, the muscles of the shoulder girdles offer no resistance and the shoulders go up to the ears. (See Plate LXXXVII. Fig. 3.)

The condition of the muscles.—There is no definite paralysis. All the movements of the body can be performed, but with much less force than in a healthy child of the same age. The muscles of the back, shoulder girdles and upper extremities (especially those of the back) are very feeble. The condition of the muscles in the different parts of the body is as follows:—

Feet.—The bony prominences of the foot stand out. When the patient is lying at rest in bed the toes are pointed. Dorsi-flexion seems to be more impaired than the other movements at the ankle joint.

Legs.—The muscles of the calves are moderately atrophied, but feel tolerably firm. The muscles of the legs are proportionately less atrophied than those of the thighs.

Thighs.—All the muscles of the thighs are markedly atrophied. The adductors seem to be more feeble than the abductors. The ...cles of the left thigh are more atrophied than those of the right.

...uttocks.—The buttocks are large in proportion to the other ...cles of the body, but not more so than they might quite well ... a healthy girl of the same age. They feel firm and elastic. ...illary tremors are occasionally seen in the buttocks.

...ack.—The muscles of the back are very feeble and markedly atrophied, especially on the right side. Fibrillary tremors quently occur in the muscles of the back.

Abdomen.—The abdominal muscles are feeble and appare... atrophied; those on the left side of the abdomen seem to be m... affected than those on the right.

Shoulder girdles.—The scapular muscles and all the muscle... the shoulder girdle with the exception of the upper part of ... trapezius are much atrophied. The deltoid on both sides is v... much atrophied; all the bony prominences of the shoulder sta... out in marked relief. The pectoralis major on both sides see... to be atrophied throughout, but the clavicular portions are slight... less affected than the sternal portions.

Upper arms.—The triceps is markedly and the biceps a... brachialis anticus are considerably atrophied in both arms.

Forearms.—All the muscles of the forearm on both sides a... much atrophied.

Hands.—The atrophy seems to involve the small muscles of th... ...ands; the thenar and hypothenar eminences are flat, and th... ...ollows between the fingers and in the palms are unusually wel... ...arked. The muscles of the left hand seem to be more affecte... ...an those of the right.

Neck.—The left sterno-mastoid is normal, the right is less pro-...nent and full and seems to be slightly affected.

...ace.—The muscles of the mouth are perhaps slightly affected; ... mouth is somewhat pouting.

...ngue.—The muscles of the tongue are unaffected.

...asurements.—The detailed measurements of the limbs were as fol...ws:—

Right arm, thickest part,	5½	inches.
Left " "	5½	"
Right forearm, "	5¼	"
Left " "	5¼	"
Right thigh, "	9¼	"
Left " "	9¼	"
Right calf, "	8¾	"
Left " "	8¾	"

...the muscles, excepting the glutei which are firm and elastic ...muscles of the calf which are moderately firm, feel soft an... ...y.

...ry tremors.—Fibrillary tremors are of frequent occurrence ...scles of the back and are occasionally seen in the scapular ...e glutei, the clavicular portion of the pectoralis major ...iceps.

... *reactions.*—All of the muscles readily react to the ...ent, but less forcibly than in health. They also con-... galvanic current, but less forcibly and sharply than ... The order of the polar reactions seems to be quite ...

...*n of the reflexes.*—A feeble plantar reflex can be ... left side, none on the right. ...ks are absent.

... eflexes are normal.

... *and trophic condition of the skin, bones and joints* is norma...

...*ions*, including the muscular sense, are normal.

The ...ties.—Normal; the patient is very bright and intellig...

...*spiratory, digestive* and *urinary systems* are normal.

Treat... ... Arsenic and strychnine (two drops of Fowler's solution ... drops of liquor strychniæ, three times daily) ... mouth; and one drop of liquor strychnine, were gi... ...sed to two drops, injected once daily into the subsequ... the ...

muscles ... loid (Burroughs, Wellcome 5-grain) was sub-... One ... ee times daily. sequent... faradic current were applied daily to the Massage ... s and back. muscles of ...

Progress ...ase.—The patient certainly gained strength under this ...nt. In the course of a month, she was able to get up fr... recumbent to the erect position, climbing up her thighs.

At the d... ...r discharge (August 18th, 1894) the fibrillary twitchings ... much less frequent in the muscles of the back and n... occurred in the other muscles (scapular muscles, tric...

After the ... discharge she remained much *in statu quo* until 5th J...6, when she was attacked with pleuro-pneumonia ... on 8th June 1896. Dr. Gill was kind enough to ob... ...ission for a post-mortem examination. It

was made by Dr. Muir, to whom my sincere thanks are due for the following exhaustive and most important report upon the condition of the muscular system, spinal cord and nerves.

Dr. Muir's Report on the Post-mortem Appearances.—'The post-mortem examination of Isabella P took place on 8th June, the patient having died on the previous day. The body was that of a girl tall and fairly well developed for her age. It was anæmic in appearance and showed a remarkable degree of general muscular wasting. The atrophy appeared most marked in the arms and shoulders, where it was of very extreme degree; it was also very great in the muscles of the chest, intercostals, etc., and also in the legs, though in them proportionately less than in the arms. The buttocks were fairly prominent, but this was found to be due to a thick layer of subcutaneous fat; the glutei were really atrophied, though less so than the other muscles. T muscles when exposed were all of pale colour—a pinkish i soft in consistence, and in many the fasciculi appeared finer t normal. Very little, if any, infiltration of fat in the substance the muscles could be detected on naked eye examination.

'The spinal cord appeared to be throughout considerably thin than it ought to be in such a subject, and the cervical and lu enlargements rather fully marked. Otherwise it showed noing abnormal. It was in good condition and was at once plac in Muller's fluid. The nerves showed nothing abnormal on e d eye examination.

'The cavities of the body were not opened.

'The *microscopic changes* were as follows:—

'*Muscular system.*—Portions of the biceps, deltoid, glut calf muscles were examined and all showed marked c For purposes of description the muscle fibres may be divid those which were of normal size or increased in size and those were of small size. The following general statement may be

'*Large Fibres.*—While many of the fibres were of norma considerable proportion were distinctly enlarged (see P Figs. 8 and 10). Some were increased to twice or th normal diameter, and, whilst some preserved their nor verse striation, others had a somewhat homogeneous appearance with irregular markings (see Plate XC. Fig showed areas or spots more faintly stained as if they were und going a degenerative softening, but these were ne o sharply defined as in the case of George P. (Case XIII.) irregular fissuring and longitudinal striation were very dis at places, and in some the swelling was irregular with cor tions and there (see Plate XC. Fig. 8). In many t sarcolemma nuclei appeared to be of normal number, but others showed marked proliferation, lying sometimes irreg arly but often in longitudinal rows. This latter arrangeme was in instances accompanied by a longitudinal splitting c the fibres narrow portions, some of which were of very sm l diamete Plate XC. Fig. 8). This proliferation of nuclei and proc splitting were specially well seen in the calf musc The enl and altered fibres occurred irregularly but were not infreq seen alongside very minute fibres. On transverse section lying singly they had usually a circular outline, but often were lying very closely opposed to one another, the outlin irregularly polygonal.

'*Small Fibres.*—Fibres of all sizes were pr down which were just visible, but a large propor were minute size, their diameter being about two or three tin of a capillary, i.e. intermediate sizes were proportiona numerous. These minute fibres were arranged in vario (a) Sometimes a bundle was formed composed almost en minute fibres of fairly regular size, with or without nuc liferation between, but with practically no fibrous increa Others were mixed with the large fibres, run ning among singly or in small groups and usually accompanied by nucl liferation which was sometimes very marked (Plate X (It was specially in the case of these that the origi of splitting from the large fibres could be though in fibres usually showed transverse striation connective some it was absent. (c) Again, others were oups or in tissue, arranged, as seen on transverse sect iculi which long rows (Plate XC. Fig. 9). These repres as just to were disappearing, some of the fibres bein red by pro- appear as mere lines often surrounded or ined faintly. liferated nuclei some of which were enlarg some cases, The connective tissue was sometimes dens fibres trans- ... between. In the smalles collections

of muscle fibres surrounded by a sheath of circularly arranged and definitely laminated connective tissue (Plate XC. Fig. 10). The fibres in the interior were of various sizes but always small and loosely arranged, and the sheath was so definite as to appear like the wall of a small vein. (These structures have already been described by Dr. Bruce as "muscle-rings.") They probably represent portions of fasciculi in process of atrophy around which a concentric arrangement of fibrous tissue has taken place, though the regularity of the sheath forms a very striking appearance.

'The change seemed to be most advanced in the deltoid and in the biceps, as in them fasciculi were in process of disappearance, only the sarcolemma nuclei surviving in places. In the calf muscle the change appeared to be in pretty active progress, and in it specially the process of splitting and formation of small fibres was well seen. In it also there was some increase of fat between the fibres. In the gluteus the change was much less advanced but was of the same nature.

'The chief changes found may thus be summarised:—

1. Many greatly enlarged fibres in which there was often marked evidence of malnutrition and degenerative change.
2. Very numerous minute fibres, many of which resulted from longitudinal splitting of larger fibres, others from simple atrophy.
3. A gradual dwindling and disappearance of the small fibres, often associated with connective tissue growth.

'*Nerves.*—The great sciatic nerve, a branch of the posterior tibial, and a branch going to the biceps were examined. In the great sciatic there appeared to be rather a preponderance of the smaller nerve fibres with, at places, a little interstitial increase of fibrous tissue and nuclear proliferation. But these changes were not at all marked and the nerves otherwise appeared quite healthy.

'*Spinal Cord.*—Portions were examined from different levels. Sections stained by Weigert Pal method showed no degeneration in any of the tracts. In the anterior cornua in the cervical region, the large multipolar cells appeared rather fewer in number than usual and the processes of some a little atrophied, but others were quite healthy. In the other parts no distinct change was found. The grey substance of the cord everywhere was much congested and there was emigration of leucocytes around the capillaries at places; this, however, was quite a recent change.'

Case XIII.—George P., aged 9, was admitted to the Edinburgh Royal Infirmary on 22nd December 1894, suffering from pseudo-hypertrophic paralysis.

Previous History.—The patient was quite strong until he was about 5 years old; he then began to stumble and fall in walking, apparently in consequence of muscular weakness in the lower extremities.

He had scarlet fever soon after the muscular weakness commenced, and influenza two years ago. He takes a cold every year which usually lasts the whole winter.

He can still walk to school (about a mile) but falls very often and gets soon tired if he runs; he himself says 'I fall an awful lot.'

State on Admission.—The patient is a bright-looking boy; his face is pale but not thin; his lips are red and he is well nourished.

Motor apparatus.—The motor power is much impaired both in the legs and arms.

The patient can rise from the recumbent position fairly well, using his arms to climb up his thighs. He walks easily, but cannot run freely. The gait is not characteristic of pseudo-hypertrophic paralysis. He can go up and down stairs pretty well but in a jerky manner, especially ascending; he seems to be tired very soon.

The back is slightly curved in the lower dorsal region. The abdomen is somewhat prominent. He is unable to fix the scapulæ to the thorax; when held up by the armpits the shoulders go up to the ears.

The condition of the muscles.—In this case the atrophy is much less marked than in cases XI. and XII.

The following muscles are atrophied:—Infraspinatus, supraspinatus, deltoid, lower part of trapezius, biceps, triceps, and the muscles on the front of the thigh. The calves are firm and apparently in some degree enlarged. The glutei are fairly large and well developed.

There are coarse fibrillary twitchings in the deltoids, latissimus dorsi, trapezius, infraspinatus and muscles on the front of the thigh.

The reaction of the atrophied muscles to the faradic current appears to be diminished—less so in the arms than in the legs.

Co-ordination is normal.

The reflexes (superficial, deep and organic) are normal.

The sensory and intellectual functions are quite normal.

The temperature is always (except as the result of temporary complications) subnormal.

The viscera are all healthy.

On *19th February* 1895, a small piece of the calf muscle was removed (with the consent of the patient's relatives), under chloroform by Mr. Cotterill, for microscopic examination. It was immediately placed in Müller's fluid and sent to Dr. Muir, who kindly examined it and reported as follows:—

'**Microscopical examination of a portion of the calf muscle.**—In this muscle there was a very striking change of a different nature to that found in the two other cases of this family. This was the presence of large vacuole-like masses of degeneration in a considerable number of the fibres. As seen on transverse section, these areas were circular or somewhat oval in shape, usually lying in the centre of the fibre and surrounded by a rim of healthy muscle substance. They had a very sharply marked outline and stained more faintly with rubin and orange than the healthy muscle substance, sometimes being slightly tinted blue with the hæmatoxylin. They appeared to be composed of a hyaline or colloid substance, and were either homogeneous in appearance or showed marked as if a process of coagulation had taken place (Plate XC. Fig. 11). Nuclei were not present in their interior. On longitudinal section they were seen to extend for a considerable distance down the centre of the fibre. In one or two instances the degenerated material lay at the periphery, enclosing a small portion of healthy substance; but this appearance was rare. Other fibres without this degeneration were swollen, badly striated and splitting irregularly. There was, however, little or no nuclear proliferation and only at one point near a tendinous attachment were there a few small fibres in process of formation by splitting. There was practically no increase of fat.'

Treatment and Progress of the case.—During the patient's stay in hospital he was treated with extract of thymus gland, arsenic and strychnine (hypodermically), massage and the faradic current.

During the two months that he was in hospital he grew 1½ inches in height and increased 7 lbs. in weight (see table). At the time of his discharge his muscular power was somewhat better than on admission.

Measurements.—The following are the detailed measurements:—

	Inches.
Right arm, thickest part,	7
Left, „ „ „	6¼
Right forearm, „ „	5¼
Left „ „ „	5
Right thigh, middle,	10¾
Left „ „	11
Right calf, thickest part,	9½
Left „ „ „	9½

	Height. Ft. Ins.	Weight. St. Lbs.
9th January 1895,	4 ¾	4 ½
29th January 1895,	4 1¾	4 3
13th March 1895,	4 2¼	4 7½

Case XIV.—Chrissie P., aged 6; was admitted to the Edinburgh Royal Infirmary on 26th May 1894, suffering from pseudo-hypertrophic paralysis in a very early stage.

Previous History.—The patient has always had a weak back; her father says she has never been able to walk well, or run and jump like other children. Since she commenced to walk, she has always been liable to stumble and fall; her knees show scars of one or two such tumbles. She has never been able to go upstairs easily, or to run up a hill, 'as it makes her tired.'

She had an attack of scarlet fever at the end of last year. She has not had any other illness; in fact, her general health has always been remarkably good. Her parents do not think that her walking has been worse since the scarlet fever.

State on Admission.—The patient is a rosy, plump, healthy, happy-looking child. She is very bright and intelligent.

The patient complains of a weak back. She is apt to fall and stumble quite unexpectedly. Her attitude in the erect position presents no peculiarity, except the presence of a slight antero-posterior curve (hollowing out of the back) in the lower dorsal and lumbar regions.

The gait is normal; the patient can run, but not freely and easily.

In getting up from the recumbent position she does not climb up her thighs, but she uses her hands more than an ordinary child would do. She has considerable difficulty in going up stairs.

When the patient is raised by the armpits, the shoulders go up to the ears.

The condition of the muscles.—The calves and buttocks are firm and apparently somewhat enlarged. The muscles of the upper extremities and shoulder girdle, especially the pectoralis major, appear to be somewhat atrophied. The infraspinati are not enlarged.

Measurements.—The detailed measurements of the limbs were as follows:—

Right upper arm, thickest part,	.	5¼ inches.
Left „ „	.	5¼ „
Right forearm, „	.	5½ „
Left „ „	.	5½ „
Right thigh, „	.	9½ „
Left thigh, „	.	9½ „
Right calf, „	.	9 „
Left „ „	.	8¾ „

The condition of the muscles.—The muscles of the calves and buttocks were firm.

Fibrillary tremors were not observed.

The electrical reactions were normal.

Reflexes.—The superficial reflexes were normal. The knee-jerks were absent.

The organic reflexes were normal.

The sensory functions, including the muscular sense, were normal.

The *circulatory, respiratory, alimentary* and *urinary systems* were normal.

The patient was discharged from the Infirmary on 18th August 1894, much *in statu quo*.

Case XV. Typical pseudo-hypertrophic paralysis.—G. M., aged 14½, was sent to me on January 17th, 1895, by Dr. Laing of Arbroath, suffering from typical pseudo-hypertrophic paralysis, and was subsequently admitted to the Edinburgh Royal Infirmary.

Previous History.—The patient's parents state that the disease commenced in early infancy. His mother noticed that he could never sit up on her arm as a strong, healthy baby should be able to do; his back, she says, always seemed weak. He did not begin to stand and walk until he was two years old. His father says that instead of walking he used to roll about the floor. His parents attributed his clumsiness and difficulty in walking to the fact that he was an unusually fat child. He has never walked well, but no marked difficulty or peculiarity in gait was noticed until he was between five and six years of age. At that time, his gait became waddling and rolling. He has never been able to go up stairs. He never could run or jump. The disease has gradually and slowly increased. Up till last year he was able to go to school; he had to walk a considerable distance to and from school; on one occasion, he said, he walked six miles. During the past year, the muscular weakness and difficulty in walking have greatly increased, and he has been for the most part confined to the house, but he can still manage to walk about with the help of a stick. His general health has always been good. He got his teeth quite easily and has never suffered from any illness whatever.

Family History.—His father and mother are strong and healthy. So far as they know, no other case of the disease has ever occurred amongst any of their relatives.

The family consists of eight children, all living; two children were born prematurely at the sixth month. The ages of the children are as follows:—

1. Premature birth at the sixth month.
2. Girl, aged 16½. When seven years of age she suffered for some time from severe inflammation of the eyes. She is now quite well. There has never been anything wrong with her walking.
3. *Boy*, aged 14½; the *patient*.
4. Miscarriage at the sixth month.
5. Boy, aged 12; quite healthy and strong.
6. Girl, aged 10; „ „
7. Boy, aged 8; „ „
8. Girl, aged 3¾; „ „
9. Boy, aged 2; „ „
10. Boy, aged 6 months; „ „

None of the other children have the slightest difficulty in walking; they can all run well, in fact the father says some of them too well.

Present Condition.—The patient is a well-grown, well-developed lad. He is unable to walk without a stick, and even then walks with great difficulty. He cannot get up from the ground, and has great difficulty in raising himself, when sitting in a chair, to the erect position. When one attempts to lift him up by the shoulders, the hands being placed in the axillæ, the shoulders go up to the ears.

Attitude in the erect position.—When placed in the erect position, the patient is able to stand and maintain his balance; the heels are raised and the legs are placed wide apart, but not in the same antero-posterior plane; the right leg is projected farther forwards than the left (see Plate LXXXVII. Fig. 7). The impression conveyed to the mind is that the right leg is longer than the left. The patient is unable to stand if the two legs are placed on the same base line (i.e. opposite to one another), even although they are widely separated.

The chest is flattened from before backwards.

Gait.—The patient is able to walk in a peculiar, rolling, crab-like way, with the aid of a stick. In walking, the back is much arched. He appears to have great difficulty in raising the foot from the ground, in bringing the leg forward, and in flexing the thigh on the abdomen. He walks better in slippers than in boots; this, he says, is owing to the boots being so heavy.

The condition of the muscles.—The calves are large and hard; they stand out very prominently. The thighs are, relatively to the calves, wasted.

The glutei muscles are enlarged; the right buttock is somewhat larger than the left.

The scapular muscles, including the infraspinati, are all markedly atrophied.

The clavicular portions of the deltoids are atrophied; the acromial portions slightly, but distinctly, enlarged.

The upper arms are thin. In both arms, the biceps and brachialis anticus are atrophied. The scapular and inner heads of the triceps are atrophied; the outer head of the triceps is distinctly enlarged.

The pectoral muscles (latissimi dorsi and serrati) are markedly atrophied.

When the arms are placed at a right angle to the body, a very marked hollow is present just below the deltoid muscle; the muscular tissue forming the posterior fold of the axilla (latissimus dorsi, teres major and teres minor) seems to have almost entirely disappeared.

The left side of the cheek is distinctly weak in comparison with the right. The patient cannot suck in the finger; he is able, however, to whistle, raise the upper lip, and close his eyes quite firmly. The tongue is not enlarged.

Measurements.—The following are the detailed measurements of the limbs, etc.:—

	Right	Left
Calf, thickest part,	12⅞	12⅝
Thigh, 7½ inches above condyle	14¼	13½
Foot, length	9½	9¼
Arm, thickest part	7⅝	7¼
„ below insertion of deltoid	7	6¾
„ just above elbow joint	6⅞	6¾
Forearm, thickest part	7¾	7¾
„ just above wrist	5¾	5¾
Length of hand from wrist to tip of middle finger	7¼	7½

There are no fibrillary twitchings and there is no reaction of degeneration in any of the affected muscles.

Reflexes.—The knee-jerks are absent.

The plantar reflex is absent.

The functions of the bladder and rectum are normal.

Vasomotor alterations.—There is marked venous mottling of the legs and thighs. The feet and hands get blue and cold when exposed, but the patient says he does not feel the cold much.

The sensory functions are normal in every respect.

The pupils are dilated, but they react perfectly to light. The fundi oculi are quite normal.

Mental functions.—The patient is of a happy and contented disposition, mentally quite acute, and, so far as intellectual development is concerned, quite up to the average standard.

Viscera.—The heart and all the internal viscera are normal.

The teeth are normally shaped. The patient's physiognomy is in no way suggestive of inherited syphilis. (The family history was suggestive of this.)

The patient is very healthy and always ready for his meals.

The genital organs are well developed.

On 19th February 1895, a portion of the calf muscle was removed (with the consent of the patient and his parents) by Mr. Cotterill under chloroform. The wound healed by first intention. The portion of muscle removed was at once placed in Müller's fluid and handed to Dr. Muir who kindly made sections of it and reported as follows:—

'**Microscopic examination of portion of calf muscle removed during life.**—This showed all the changes usually met with in pseudo-hypertrophic paralysis (see Plate XC. Fig. 12). There was great lipomatosis between the strands of muscle fibres and some of the fibres seemed pressed upon and indented at places. As regards the muscle fibres, some were enlarged and had a uniform appearance, the striation having disappeared; others were healthy in appearance. Some showed nuclear proliferation and a process of splitting could also be traced. Some were of minute size and these were usually well striated. Fibres of different sizes were irregularly arranged in strands of varying breadth which ran between the fat-cells. Around some of the fibres there was connective tissue overgrowth. The sections showed, therefore, a typical picture of the changes characteristic of the disease.'

Treatment and Course.—The patient remained for several weeks in hospital. He was treated with extract of thymus gland, arsenic, strychnine (hypodermically), massage and the faradic current.

He was discharged on 14th March 1895. He stated that he felt stronger, but the walking power was distinctly worse.

On *10th October* 1896, Dr. Laing, under whose care the patient is, kindly sent me the following note of the present condition:—'He keeps very well in health, is cheery and bright; his appetite is good. The legs are quite useless, he wheels himself about the house in a wheeled chair; during the summer he used a specially constructed tricycle outside. The arms seem quite strong.'

Case XVI. Myopathic muscular atrophy affecting the face, tongue, palate, ocular muscles, the muscles of the head, neck, shoulder girdle and upper extremities.

This case is a very peculiar one. For the reasons given below, I am disposed to think that it is probably a case of myopathic muscular atrophy of irregular type, but the diagnosis is, I admit, a matter of grave difficulty. The notes are as follows:—

Miss A., aged 26, was seen with Dr. Cullen of St. Boswells on 10th April 1895, complaining of difficulty in speaking and swallowing, and weakness and wasting of the muscles of the head, neck, and upper extremities.

Previous History.—The patient first consulted me on 3rd June 1890. She then complained of weakness in the upper extremities—difficulty in moving her arms, in holding anything heavy and in lifting objects. This muscular weakness commenced, she said, gradually and without obvious cause about a year previously (beginning of 1889). She also stated that at times she felt some difficulty in speaking. In February last she saw double for a month—obviously the result of weakness or paralysis of some of the ocular muscles—but she stated that her eyes were not twisted. Before her illness commenced she used to suffer occasionally from neuralgia in the head (apparently ordinary tic).

At this time (June 1890), although the upper extremities were obviously weak and the muscles of the upper extremities somewhat flabby and ill nourished, I did not detect any definite localised atrophy, and there was no definite paralysis. All the individual movements could be performed, but less powerfully than normal.

I could not detect any paralysis in the ocular or facial muscles, and there was no obvious cause for the difficulty in articulation with which, she said, she was occasionally, but merely temporarily, affected.

The lower extremities were unaffected. The reflexes were normal.

The general health was good. The viscera were all healthy.

A tonic containing strychnine and arsenic, massage and electricity, were prescribed.

I heard nothing more of the patient until she was brought to me by Dr. Cullen on 10th April 1895.

During the five years which have elapsed since I first saw her the muscular weakness has got slowly but steadily worse. Dr. Cullen states that at times the face is quite expressionless, and that she sometimes squints horribly.

Present Condition.—There is marked flatness of the face, the expression of which is highly suggestive of the facial form of myopathic atrophy. The lips are pouting. The patient cannot whistle. There is distinct weakness of the orbicularis palpebrarum, especially the left. There is no definite squint, but the internal recti are weak and the associated movements are not quite co-ordinately performed.

Articulation is somewhat thick. The tongue can only be partly protruded. It is irregularly atrophied, presenting some slight irregularity on the surface—much less marked but apparently identical with the condition depicted in this Atlas (vol. i. Plate XIII.), in a patient suffering from bulbar paralysis.

The patient says that she has considerable difficulty in swallowing both solids and fluids; fluids occasionally regurgitate through the nose. The soft palate appears to be partly paralysed; the larynx is normal.

The muscles of the head and neck are very weak. She states that the head feels as if it would fall off. When she stoops forward (sitting in the writing position) it falls down and she is unable to raise it.

The muscles of the neck are markedly atrophied.

The upper extremities are very feeble, but most of the movements can be performed. The grasping power of the right hand, as measured by the dynamometer, equals 10 and that of the left 0. Pronation and supination of the forearms are fairly well performed. The power of flexing and extending the elbow joints is very much impaired. She cannot raise the arm to the horizontal position or keep it raised (paralysis of deltoid).

The muscles of the thumb and hand are distinctly atrophied; those of the forearm slightly so; those of the upper arm markedly so.

Though both deltoids are almost completely powerless, they are distinctly enlarged and obviously in a condition of pseudo-hypertrophy; they feel firm and elastic, as in cases of pseudo-hypertrophic paralysis and myopathic atrophy.

The scapular muscles and the muscles attaching the scapulæ to the spine appear to be atrophied. The patient cannot fix the scapulæ to the thorax; when raised by the arms under the axillæ, the shoulders go up to the ears.

The muscles of the lower extremities are unaffected.

The patient can raise herself from the ground without climbing up the thighs.

The gait is normal.

There are no fibrillary twitchings, and all the affected muscles respond, though feebly, to the faradic current.

The knee-jerks are present though less active than in health.

The bladder and rectum are unaffected.

There are no sensory disturbances of any kind.

The intellectual faculties are unaffected.

The patient is slightly anæmic, but the general health is good. The viscera are all healthy, but the action of the heart is somewhat thumping.

Diagnosis.—The diagnosis was difficult. In many of its features the case resembled a central (nervous) rather than a peripheral (myopathic) lesion. But the distinctly hypertrophied, or rather pseudo-hypertrophied, condition of the deltoids seemed to show that the case was one of myopathic muscular atrophy.

If this opinion is correct, the case is certainly a most peculiar one. The affection of the ocular muscles, of the tongue and of the palate are, so far as I know, rarely if ever observed in cases of myopathic atrophy.

Prognosis.—A very unfavourable prognosis was given.

Treatment.—The patient was advised to continue the arsenic, strychnine and electricity.

Subsequent course.—On 17*th August* 1895, Dr. Cullen kindly wrote me saying that the deltoids were much smaller, the condition otherwise the same.

Condition, August 1896.—I heard nothing more of the patient until August 1896, when Dr. Cullen informed me that she was distinctly better and that in his opinion the improvement was entirely due to the hypodermic injection of strychnine which had been steadily and persistently persevered with.

Case XVII. Typical pseudo-hypertrophic paralysis.

J. A., aged 8, was admitted to Ward 27, Edinburgh Royal Infirmary, on 18th March 1895, complaining of general weakness and difficulty in walking.

Previous History.—When a year old he had whooping-cough. He did not begin to walk until he was two years old. As an infant he never could creep as a healthy child does. When 3½ years old his abdomen became swollen, probably as the result of some tubercular affection; he was confined to bed for many months and became much emaciated. He recovered very slowly from this illness. When he again began to walk he walked in the peculiar pseudo-hypertrophic way that he does now. He has never been able to walk more than 500 or 600 yards. At the age of 5 he had a mild attack of scarlet fever. At the age of 7 he had a slight attack of measles. His walking has been much worse since that date. Of late years his general health has been very good.

His social surroundings have been most satisfactory in every respect.

Family History.—His father and mother are both active and healthy.

The family, which consists of seven children, seems to be scrofulous. No other members are affected with pseudo-hypertrophic paralysis. The ages are as follows:—

1. Girl, aged 20, perfectly healthy.
2. Girl, aged 18, never very robust since a severe attack of scarlet fever when two years old.
3. Girl, aged 16, perfectly healthy.
4. Boy, aged 13, looks perfectly healthy; had an abscess of the elbow joint.
5. Girl, aged 10, perfectly healthy; two years ago had pains and weakness in the legs; now quite well.
6. Boy, aged 8; the *patient.*
7. Boy, aged 2½ years; perfectly healthy.

So far as is known, no near relatives have suffered from pseudo-hypertrophic paralysis or any other form of nerve disease.

Present Condition.—Is small for his age but looks healthy; is fat and well nourished. Cicatrices, the remains of former glandular abscesses, are present near the angle of each jaw.

Temperature subnormal.

Posture in the erect position.—The patient stands with his legs wide apart, the heels slightly drawn up and the feet slightly inverted. The back is markedly curved, the abdomen and chest are very prominent, the shoulders are drawn back and the arms are kept slightly out from the sides.

Gait.—This is characteristically waddling.

Co-ordination is perfect, but the muscular power is so feeble that the slightest touch makes the patient fall when he is in the erect position.

Muscular power.—This is very feeble. When the patient attempts to sit down or to get down to the ground from the erect position, he falls all of a heap as soon as the knees are bent.

He is unable to get up from the ground, or even to turn from his back on to his face when lying flat on the ground.

When raised by the shoulders the arms go up to the ears.

Condition of the muscles.—The patient looks a remarkably muscular boy. The calf muscles, the muscles of the thigh (quadriceps and hamstring muscles), the glutei and the infraspinati, deltoids and tricipites are markedly enlarged, firm and hard. The muscles of the back are also enlarged.

The pectoralis major and biceps are atrophied.

The enlarged muscles are all very feeble.

There are no fibrillary twitchings.

All the muscles, but especially those which are enlarged, respond feebly to both forms of current. But there is no trace of the reaction of degeneration.

Reflexes.—The knee-jerk on the left side is quite absent, that on the right just perceptible—very markedly diminished.

The superficial reflexes are active.

The organic reflexes (bladder and rectum) are normal.

The *sensory functions* are quite normal.

Intellectual faculties.—Quite normal. The patient is bright, cheerful and very intelligent. Although he has only been at school for a year he reads fairly well.

The *circulatory*, *respiratory*, *digestive* and *urinary systems* are quite normal.

Treatment and Progress of the Case.—The patient was treated with massage, electricity and thymus extract (five grains three times daily).

He remained in hospital until 25th April and was discharged *in statu quo.*

DESCRIPTION OF PLATE XC.

MICROPHOTOGRAPHS OF MUSCLES IN PSEUDO-HYPERTROPHIC PARALYSIS AND MYOPATHIC ATROPHY.

Fig. 1.—Transverse section of a portion of the deltoid muscle excised during life in Case I.—typical pseudo-hypertrophic paralysis. Magnified 50 diameters. (See Plate LXXXVII. Figs. 1 and 2, and page 95 for description of the clinical history and microscopic appearances in the muscle.)

Numerous darkly-stained muscular fibres (to which the letter R points) are seen in groups, separated by a large quantity of fat and connective tissue (to which the letter Q points).

Fig. 2.—Longitudinal section of a portion of the deltoid muscle excised during life in Case I.—typical pseudo-hypertrophic paralysis. Magnified 60 diameters. (See Plate LXXXVII. Figs 1 and 2, and page 95 for description of the clinical history and microscopic appearances in the muscle.)

Numerous darkly-stained muscular fibres, some of normal size, some much smaller than normal (to which the letter J points), are seen in longitudinal section, separated by a large quantity of fat and connective tissue (to which the letter K points).

Fig. 3.—Longitudinal section of a portion of the calf muscle removed after death from Case IV.—pseudo-hypertrophic paralysis ending in extreme muscular atrophy. Magnified 80 diameters. (See Plate LXXXVIII. Figs. 1 and 2; also page 98 for description of the clinical history and microscopical appearances in the muscle.)

Several minute (atrophied) muscular fibres (to which the letter N points) are seen in longitudinal section, in some of them the transverse striation is still perfectly preserved. The muscular fibres are separated by a large quantity of fat-cells and connective tissue (to which the letter O points).

Fig. 4.—Transverse section of a portion of the calf muscle removed after death from Case IV.—pseudo-hypertrophic paralysis ending in extreme muscular atrophy. Magnified 80 diameters. (See Plate LXXXVIII. Figs 1 and 2; also page 98 for description of the clinical history and microscopical appearances in the muscle.)

Groups of muscular fibres of various sizes (to which the letter M points) are seen in transverse section. The muscular fibres are separated by a large amount of fat and connective tissue (to which the letter L points). In the centre of the figure a vessel is situated.

Fig. 5.—Transverse section through a fasciculus in a portion of the biceps muscle removed during life in Case XI.—pseudo-hypertrophic paralysis and myopathic atrophy. Magnified 250 diameters. (See Plate LXXXIX. Figs. 1 and 2, and page 106 for description of the clinical history and microscopic appearances in the muscles.)

The letter F points to two very large (hypertrophied) muscular fibres, the letter G to a minute fibre.

Throughout the section a number of very small (atrophied) transversely divided muscular fibres are seen; the muscular fibres are separated by a slight excess of connective tissue which is richly nucleated; there is no lipomatosis.

Fig. 6.—Longitudinal section through a portion of the biceps muscle removed during life in Case XI.—pseudo-hypertrophic paralysis and myopathic atrophy. Magnified 50 diameters. (See Plate LXXXIX. Figs. 1 and 2, and page 106 for description of the clinical history and microscopic appearances in the muscle.)

A number of muscular fibres which are of normal size or somewhat enlarged (to which the letter D points), are seen in longitudinal section. The letter E points to a very richly nucleated tissue in which a large number of extremely small (atrophied) fibres are situated. Under this power the atrophied fibres are seen as faint lines. On the extreme left-hand side of the figure two of these minute fibres, surrounded by nuclei, are seen lying between two muscular fibres of normal size.

Fig. 7.—Longitudinal section through a portion of the biceps muscle removed during life in Case XI.—pseudo-hypertrophic paralysis and myopathic atrophy. Magnified 250 diameters. (See Plate LXXXIX. Figs. 1 and 2, and page 106 for description of the clinical history and microscopic appearances in the muscle.)

The letter I points to a large (hypertrophied) muscular fibre which is homogeneous in structure, but which shows traces of longitudinal fissuring. In the centre of the figure several small (atrophied) muscular fibres surrounded by a large excess of nuclei are seen.

Fig. 8.—Longitudinal section through a portion of the calf muscle removed after death from Case XII.—extreme myopathic muscular atrophy. Magnified 250 diameters. (See Plate LXXXVII. Fig. 4, and pages 107 and 108 for description of the clinical history and post-mortem appearances.)

A greatly enlarged (hypertrophied) muscular fibre (to which the letter C points) is seen in longitudinal section. A very minute (atrophied) fibre, apparently formed by splitting, and surrounded by an excess of nuclei, is separated from the large (hypertrophied) fibre by a fibre of medium size. The hypertrophied fibres, which have for the most part lost their transverse striation, are in places apparently undergoing a colloid or hyaline degeneration, and show irregular fissuring accompanied by nuclear proliferation.

Fig. 9.—Longitudinal section through a portion of the deltoid muscle removed after death from Case XII.—extreme myopathic muscular atrophy. Magnified 250 diameters. (See Plate LXXXVII. Fig. 4, and pages 107 and 108 for description of the clinical history and post-mortem appearances.)

The letter T points to a large (hypertrophied) muscular fibre; the letter U to a minute (atrophied) muscular fibre, in which the transverse striation is perfectly preserved. Some still more minute fibres which retain their transverse striation are seen in the middle of the section, other minute fibres are completely degenerated or replaced by fibrous tissue. There is some excess of connective tissue, but no fat between the degenerated muscular fibres. The muscular fibres are in places surrounded by an excess of nuclei.

Fig. 10.—Transverse section through a portion of the biceps muscle removed after death from Case XII.—extreme myopathic muscular atrophy. Magnified 250 diameters. (See Plate LXXXVII. Fig. 4, and pages 107 and 108 for description of the clinical history and post-mortem appearances.

The letter A points to muscular fibres which are moderately enlarged (hypertrophied); some of the enlarged fibres contain a slight excess of nuclei. The letter B points to a 'muscle ring.' In the centre of this ring a number of small muscular fibres, in which there is an excess of nuclei, are situated. The wall of the ring is composed of a richly nucleated fibrous tissue and resembles the wall of a vein. Between the muscular fibres there is a slight excess of connective tissue, but no fat-cells.

Fig. 11.—Oblique (longitudinal-transverse) section through a portion of the calf muscle removed during life in Case XIII.—pseudo-hypertrophic paralysis or myopathic muscular atrophy. Magnified 250 diameters. (See page 108 for description of the clinical history and microscopical appearances in the muscle.)

In this case the clinical symptoms were suggestive of pseudo-hypertrophic paralysis in an early stage, but the microscopical appearances in no way resemble that condition.

The section shows greatly hypertrophied muscular fibres, many of which are extremely degenerated. In the centre of these degenerated fibres a clear space, filled with colloid or hyaline material (to which the letter S points), is seen.

Fig. 12.—Longitudinal section through a portion of the calf muscle removed during life in Case XV.—typical pseudo-hypertrophic paralysis. Magnified 50 diameters. (See Plate LXXXVII. Fig. 7, and page 110 for description of the clinical history and microscopical appearances in the muscle.)

Bundles of muscular fibres, some of them of normal size, some slightly enlarged, some considerably atrophied, are seen in longitudinal section. The muscular fibres are separated by a large quantity of fat and connective tissue (to which the letter P points).

CYANOSIS AND CONGENITAL HEART DISEASE

THE case which is represented in Plate XCI.[1] was a typical example of congenital heart disease. The patient was under the care of Dr. Limont of Newcastle-on-Tyne, to whom I am indebted for allowing my artist Mr. Williamson to paint it. There was marked cyanosis and a loud systolic murmur over the position of the pulmonary artery—in short, the case seemed to be one of congenital stenosis of the pulmonary orifice.

Morbid Anatomy.—Stenosis or complete occlusion (atresia) of the pulmonary orifice or pulmonary artery, with secondary changes in the heart, such as a patent foramen ovale or an imperfect intraventricular septum, is the condition which is present in the great majority of cases of congenital heart disease. The stenosis usually results from inflammation during fœtal life; but it may probably also be due, as Peacock has suggested, to defective development of the branchial arch from which the ductus arteriosus is formed. As a result of such a condition, the pulmonary artery would of course receive a much smaller supply of blood than normal, and would consequently be imperfectly developed.[2]

Stenosis of the pulmonary artery may also, of course, result from disease after birth.

In some cases it is extremely difficult, from the mere pathological characters of the lesion, to say whether the stenosis belongs to the congenital or the acquired form of the disease. When the lesion is limited to the valve segments and basal ring, the condition is probably acquired, for fœtal endocarditis is rarely so limited. Further, the congenital form of the disease is generally, if not always, attended by other changes, such as alterations in the trunk of the pulmonary artery, the sinus arteriosus of the ventricle, and the persistence of some of the fœtal openings in the heart. Kussmaul, quoted by Lebert, sums up the points of distinction between the two forms in the following propositions:—This affection of the heart is the more surely congenital:—1st, when the birth was near the normal end of pregnancy; 2nd, the sooner after birth cyanosis and other tokens of heart disease, collectively called physical symptoms of stenosis of the pulmonary artery, are perceived; 3rd, when the foramen ovale and the ductus arteriosus Botalli are both open, or, indeed, only the latter; 4th, when the opening of the foramen ovale is proportionately large, the ductus being closed, and especially when its size depends on want of the fleshy substance of the septum; 5th, when the valves of the pulmonary artery show anomalies of structure that are evidently congenital; 6th, when the trunk of the pulmonary artery is decidedly contracted and its walls are too thin; 7th, when the right ventricle appears contracted or stunted.[1]

The appearances which are met with in congenital stenosis differ very considerably in different cases. The most common condition is that in which the pulmonary artery is distinctly differentiated from the aorta, and narrowed or completely occluded. In cases of this description the valve segments may be fused together, or irregular in development; the foramen ovale is usually patent, the ductus arteriosus is in some cases open, in others closed; there is sometimes a deficiency in the intra-ventricular septum.

In other cases, the stenosis is chiefly situated in the right conus arteriosus, which may appear to be a third ventricle cut off from the other two. In cases of this description, the intra-ventricular septum is usually deficient, the foramen ovale usually open, the ductus arteriosus sometimes open, sometimes closed. The trunk of the pulmonary artery is usually constricted, and the coats of the vessel thinner than normal.

In a third group, still more striking anomalies are found. In some, the division of the common truncus arteriosus into the pulmonary artery and aorta is incomplete; in others, in addition to the stenosis or complete occlusion of the pulmonary artery, the heart may only consist of two cavities, or, there may be one ventricle and two auricles, or two ventricles and one auricle; in others again, in addition to the stenosis of the pulmonary artery, the aorta and pulmonary artery are transposed, or have some other abnormal connections with the heart.

Pathological Physiology.—In cases of congenital stenosis of the pulmonary artery, the secondary results produced in the heart and the manner in which compensation is established vary in different cases. They depend chiefly upon the period of intra-uterine life at which the stenosis of the pulmonary artery is established.

When the stenosis of the pulmonary artery is produced before the end of the third month of intra-uterine life, i.e. before the separation of the two ventricles is completed, the intra-ventricular septum remains imperfect, the aperture between the two ventricles being a round hole with smooth edges. In cases of this description, the blood which ought to pass after birth from the right ventricle through the lungs to the left ventricle, makes its way directly, i.e. by a short cut, from ventricle to ventricle through the aperture in the intra-ventricular septum. The blood finds its way either through the ductus arteriosus or, if, as is more frequently the case, that vessel is closed, through some of the branches of the aorta (usually

[1] The coloured Plate Cyanosis, issued with Part 2, Vol. III, is erroneously numbered XC. The reader is requested to number it XCI.

[2] The greater liability of the right side of the heart to endocarditis and myocarditis during intra-uterine life is probably due to the fact that before birth the valves on the right side are subjected to greater strain than those on the left. Peacock further supposes that in consequence of the temporary alterations of the blood pressure which are apt to occur in the umbilical arteries and placenta, disease at the base of the pulmonary artery (which is directly continuous with the descending aorta and umbilical arteries) may be established, just as disease of the base of the aorta and aortic valves may result in after life from increased blood pressure (sudden strain, etc.), within the systemic arterial system.

[1] Ziemssen's *Cyclopædia*, vol. vi. p. 318.

the bronchial, œsophageal, the anterior coronary or pericardial arteries) inosculating with branches of the pulmonary arteries.

When the lesion is produced after the third month, the intra-ventricular septum is closed and compensation is effected by the foramen ovale remaining patent. After birth the blood, instead of passing from the right ventricle through the lungs to the left heart, passes directly from the right to the left auricle—in other words, follows the course of the circulation in the fœtus. In these cases, the lungs are supplied with blood either through the ductus arteriosus remaining patent, or, if that vessel is closed, through the inosculation between branches of the aorta and the pulmonary artery.

In both classes of cases compensation is seldom perfect. The superficial veins are usually enlarged and more or less cyanosis is generally present. The balance of compensation, too, is easily upset; any slight pulmonary affection, for example, is sufficient to cause a great increase in the cyanosis and, it may be, produce other symptoms.

The condition of the right ventricle varies in different cases. In some it is markedly hypertrophied; in others, as for example in those cases in which the pulmonary orifice is completely occluded, it may be much smaller than normal or quite rudimentary. The lungs are usually found to be anæmic.

In those cases in which the patients survive to the age of puberty, chronic tubercular changes in the lungs are of frequent occurrence and are in a large proportion of cases the immediate cause of death.

Clinical History.—Cases of congenital stenosis may be conveniently divided into three clinical groups or types, namely:—

First group.—Cases in which the lesion is very severe, and in which the patient dies immediately or soon after birth.

In the most severe cases of this description, the child dies asphyxiated immediately after birth; in some cases, life is prolonged for a few weeks or months. Cyanosis is very prominent, and is very much increased by anything, as for instance coughing or crying, which further embarrasses the lungs or right heart. The temperature is usually subnormal. Somnolence is a characteristic symptom; in one case, for instance, which came under my own observation, the child would sleep for eighteen or twenty-four hours at a stretch. Dropsy of the feet may develop; shortness of breath and pulmonary complications are often present; convulsions are not uncommon.

Second group.—Cases in which the lesion is less severe, and in which life may be prolonged for several years, but in which there are from the first, symptoms indicative of the cardiac lesion.

In cases of this description there is more or less cyanosis, which may, however, only be noticeable on coughing, crying, etc., or when the right heart and pulmonary circulation become embarrassed by any sudden effort, attacks of bronchitis or other lung complications. The blueness is most noticeable in the peripheral parts of the body; the superficial veins are usually prominent. The child develops slowly, and looks much younger than his years. Shortness of breath on exertion, and palpitation are generally prominent symptoms; pulmonary complications, such as attacks of bronchitis and hæmoptysis are frequent; headache, giddiness, or even epileptiform convulsions (the result of deranged cerebral circulation) are sometimes seen. Dropsy is seldom present in cases of this description until compensation fails, or unless the venous circulation becomes suddenly seriously embarrassed by some acute intercurrent complication, such as bronchitis, endocarditis, etc. In the cases included under this group, there is usually great susceptibility to cold and all injurious external influences; the mental development of these patients may be retarded; and if they survive the trying ordeal of puberty, they are very apt to die in early manhood—between the ages of fifteen and twenty-five—from phthisis. The lung disease, as a rule, runs a protracted course; the left lung is usually the first to be attacked; repeated attacks of hæmoptysis are common.

In exceptional cases included under this group, life may be prolonged for many years. Lebert, for example, mentions that in one case of undoubted congenital stenosis, the patient attained the age of sixty-five years.[1]

Third group.—Cases in which the lesion is slight.

In cases of this description, the cyanosis and the other characteristic symptoms of congenital heart disease are slight or entirely absent. Years after birth cyanosis and shortness of breath and the other indications of a right-sided lesion may arise, and are usually due either to the failure of compensation, which has hitherto been perfect, or to the occurrence of acute endocarditis, bronchitis or some other pulmonary complication. When the pulmonary stenosis is acquired the same symptoms may of course arise.

In cases of cyanosis and congenital heart disease, as Dr. George Gibson has recently shown, the peripheral blood (blood drawn from the finger-tip, ear, etc) contains an excessive number of red corpuscles. The exact cause of the excess, whether due to an actual increase of the red blood corpuscles, to a relative increase of the corpuscles in comparison with the blood serum, or to a concentration of the red blood corpuscles in the peripheral parts of the body, has not as yet been definitely determined.

Physical Signs.—In cases of congenital heart disease with cyanosis, a systolic murmur can generally be heard over some part of the præcordial area; its point of maximum intensity varies in different cases, but is usually situated in the second and third left interspaces; in many cases the murmur is a loud one, and may be heard all over the præcordia.

It must be remembered that the exact significance of a systolic murmur in cases of congenital heart disease is not always clear. In some, it is probably due to 'fluid veins' formed as the blood passes through the constricted pulmonary orifice; in cases of this description the pulmonary second sound is feeble, altogether absent, or replaced by a diastolic murmur. In others, it is perhaps due to the passage of the blood through the patent foramen ovale[2] or through an aperture in the intraventricular septum. In others, again, it is the result of mitral or tricuspid regurgitation.

A systolic thrill can in some cases be felt over the region of the murmur. When the right ventricle is enlarged, as it is in many cases, increased dulness over the region of the right heart and (in some cases) bulging of the præcordial region are present.[3]

[1] Ziemssen's *Cyclopædia*, vol. vi. p. 317.

[2] In this case the murmur would be presystolic rather than systolic.

[3] As has been previously stated, the right ventricle is not hypertrophied or dilated in all cases of congenital stenosis of the pulmonary artery. When, for example, the occlusion is complete it may be smaller than normal; when, again, the intra-ventricular septum is imperfect, there may be no alteration in the size of the right heart.

The superficial veins are in many cases prominent. In almost all cases, they become markedly engorged on crying, coughing, etc. In some cases there is true venous pulsation in the veins of the neck.

The radial pulse is usually small and weak.

Diagnosis.—In those cases in which a systolic murmur having its point of maximum intensity in the pulmonary artery and apparently due to organic changes and not merely the result of functional conditions, is present, the question naturally arises whether the murmur is the result of congenital malformation or disease acquired after birth. In some cases it is difficult to come to a definite conclusion on this point, for, as we have previously seen, it occasionally happens that a congenital lesion of the pulmonary artery remains entirely latent for some years, and is not attended by any symptoms until several, it may be many, years after birth. In cases of this description, it might easily be supposed that the lesion was an acquired one; in fact, in many cases this is actually the case, as for example in those cases in which the congenitally malformed valve is subsequently attacked by acute or subacute endocarditis. On the other hand, it should be remembered that cases of acquired stenosis of the pulmonary artery are extremely rare.

The differential diagnosis of acquired and congenital stenosis of the pulmonary artery must, therefore, be determined by making a careful inquiry into the history of the case. Cyanosis, shortness of breath, attacks of bronchitis in early life, are very strongly in favour of the congenital variety. The family history should be inquired into, for it is not uncommon to find more than one member of a family dying from, or affected with, congenital heart disease. It is only when the symptoms and signs of cardiac disease have been entirely absent in early life that the diagnosis of acquired pulmonary stenosis can be entertained.

It must further be remembered that marked cyanosis and secondary changes in the right heart, such as dilatation, hypertrophy and tricuspid regurgitation, are frequently the result of primary lung disease, e.g. cirrhosis, chronic bronchitis and embolism, and of mitral stenosis; and since bronchitis and other pulmonary lesions are of frequent occurrence in cases of congenital heart disease, the differential diagnosis of these two groups of cases is in some cases difficult.

In congenital heart disease, i.e. such as pulmonary stenosis, the physical condition of the heart and a careful investigation into the previous history of the case usually enable a correct opinion to be formed. In pulmonary stenosis, a systolic murmur in the region of the pulmonary area is usually present and the second pulmonary sound is faint, entirely absent, or replaced by a diastolic murmur; whereas, in cases of mitral stenosis or primary lung disease, a systolic murmur in the pulmonary area is usually absent and the second pulmonary sound is loudly accentuated. Of course, in cases of complete atresia of the pulmonary orifice a pulmonary murmur will not be present, but cases of this description so rarely survive (and even if they do survive they are usually attended with such prominent symptoms continuously from the time of birth) that they can hardly give rise to any difficulty in diagnosis. In the majority of cases of pulmonary stenosis, a history of shortness of breath and more or less cyanosis from the time of birth can be elicited. But this is not absolutely conclusive of congenital heart disease, for cases are sometimes met with in which there is marked cyanosis with secondary hypertrophy and dilatation of the right heart and eventually tricuspid regurgitation and dropsy, in which these symptoms date back from childhood, and in which, therefore, the history is suggestive of congenital heart disease. In cases of this kind, reliance must chiefly be placed upon the condition of the heart as elicited by physical examination.

The degree of cyanosis is also an important point. It is usually more marked in cases of congenital heart disease than in the acquired cases. Further, in cases of congenital heart disease dropsy is often entirely absent; whereas, in advanced cases of mitral stenosis with marked cyanosis and secondary changes in the right heart, dropsy is much more frequently present.

Prognosis.—In the great majority of cases of congenital heart disease, such as stenosis of the pulmonary artery, in which the lesion is severe, the patients usually die soon after birth; and even in those cases in which they attain the age of puberty, they usually succumb during early adult life, tuberculosis of the lungs being, as I have already stated, a frequent cause of death. A few cases live to middle life, and one case has actually been recorded in which the patient reached the advanced age of sixty-five.[1]

The prognosis is of course most unfavourable in those cases in which the cyanosis is most marked; in other words, the degree of the cyanosis is, other things being equal, a fairly good criterion of the severity of the lesion.

Treatment.—Children affected with congenital heart disease should be carefully protected from cold and other injurious external influences. Anything, such as sudden efforts, which increases the cyanosis, i.e. the embarrassment of the right heart and venous circulation, and interferes with the action of the lungs, must, so far as possible, be avoided.

The usual therapeutic measures which are advisable in the treatment of chronic valvular lesions of the left heart with engorgement of the lungs and right heart, must be carried out in accordance with the special requirements of each individual case. During the acute exacerbations, oxygen inhalations may be employed.

[1] Lebert, Ziemssen's *Cyclopædia*, vol. vi. p. 317.

DESCRIPTION OF PLATE XCI.

THIS Plate represents a typical case of congenital heart disease, probably stenosis of the pulmonary artery, which was unde the care of Dr. Limont in the Royal Infirmary, Newcastle-on-Tyne. The patient was a girl aged 5; the face was markedl cyanosed; the fingers extremely clubbed and cyanosed; the cyanosis had been present since birth. The heart was situated in th right chest; the liver was on the right side of the body; a systolic murmur was audible both at the apex and base of the hear The cyanosis is extremely well portrayed in the drawing.

DESCRIPTION OF PLATE XCII.

THIS Plate represents the facial appearance in a case of chronic mitral disease—regurgitation with great hypertrophy an dilatation of the left ventricle. The patient came under my notice in the Edinburgh Royal Infirmary some years ago.

The yellow tint of the skin and the somewhat cyanotic condition of the lips and ears are well brought out in the drawin but the artist has failed to catch the languid expression and rather swollen and bloated appearance of the face.

A REMARKABLE CASE OF CALCAREOUS DEGENERATION OF THE HEAR AND ARTERIES WITH RAPIDLY DEVELOPED SYMMETRICAL SUB CUTANEOUS TUMOURS IN THE AXILLÆ, ELBOWS, GROINS, NATAI FOLDS AND POPLITEAL SPACES, AND SYMPTOMS SUGGESTIVE OI ADDISON'S DISEASE, in a Young Man, aged 25, affected with Advanced Cirrhosi of the Left Kidney, the Right Kidney having been completely destroyed fourtee years previously by Pyelonephritis.

THIS is perhaps the most remarkable case which has come under my notice during the twenty-seven years that I have been in practice. The notes are as follows :—

Mr. A., aged 25, unmarried, was seen with Dr. Menzies on April 16th, 1894. He complained of extreme debility, loss of flesh and the presence of symmetrical swellings in the axillæ, elbows, groins, inguinal folds and popliteal spaces.

Previous History.—The history which I obtained of the previous illness and his previous state of health was as follows :—

When eleven years of age, he had a severe illness, as to the exact nature of which he and his friends are unable to give any definite information. He states that he was feverish and drowsy and that he remembers doing little else but sleep all day; there was no diarrhœa and no cough. He was confined to bed for six months. He then began to improve and ultimately got quite well.

After recovering from this illness, he enjoyed good health until he went to America *eighteen months ago.* He first went to Dakota where he stayed for a short time; then to Winnipeg to take a situation.

In Winnipeg, he was subjected to great hardships, was badly fed, half-starved, and badly clothed. He had to sleep out for three weeks in a small tent on the bare ground, and to live entirely upon bread and tea. The result was that he completely broke down and was laid up for six weeks. During this illness, he lost a stone and a half in weight, and became very weak and pale. He has never been quite well since.

In December 1892, he came home and remained with his friends in Edinburgh for a year. During this time, he did not make any definite complaint and did not think it necessary to consult a doctor. His friends, who did not see anything specially wrong with him, thought that he was not sufficiently active in trying to find employment. This, he says, was because he did not 'feel up to the mark.'

Three months ago (about the middle of January 1894), he bought an engineer's business in Glasgow. After going to Glasgow, he went through a lot of hard physical work, fitting up his workshop and lifting heavy machinery. *He states that during this time he did not feel anything amiss.*

Three weeks ago, when lifting a heavy piece of machinery, he strained his back. He states most definitely that until this strain he neither felt weak nor short of breath, and that he was quite equal to the heavy physical work in which he was engaged. The strain of the back was so severe that he had to go home to bed. The next day he was no better, and, thinking that if he had to be laid up for some days it would be better to be laid up at his home in Edinburgh than in lodgings in Glasgow, he came to Edinburgh. Two days after his arrival in Edinburgh he was see by Dr. Menzies who noticed that he was pale, but as he had alway been pale no importance was attached to this fact. At this visi Dr. Menzies examined him carefully, and being unable to detec any evidence either of external or internal disease, concluded tha the weakness was the result of overwork and that the pain in th back of which he complained was due to the strain described above

A week later, he experienced pains in the muscles of the thigh and legs, in the knee-joints and in the soles of the feet; thes pains were thought to be rheumatic in nature.

A few days after this, he directed Dr. Menzies's attention to th condition of the axillæ, groins, gluteal folds and popliteal spaces.

On examining the parts, Dr. Menzies found that the skin an subcutaneous tissues were infiltrated, hard and brawny. Th appearance was quite peculiar; Dr. Menzies had never seen any thing like it before. Both Dr. Menzies and the patient stat most positively that these swellings were not present when he firs arrived in Edinburgh. The patient thought that they were du to his having worn his pyjamas for two or three days continuously he suggested that the pyjamas had irritated the affected parts.

In the course of the next week or ten days, the debility and anæmi rapidly increased and the subcutaneous swellings increased in size It was now found that the urine contained a slight trace of albumi and a few pus corpuscles.

Family History.—There was no suspicion or history of syphilis The patient's mother died of abdominal cancer and his father c bronchitis. The family consisted of six children. One brothe died of phthisis. The four remaining members of the family—tw brothers older than the patient, and two sisters—are all healthy and strong. So far as is known, the patient does not inherit tendency to any special form of disease.

Present Condition.—I found the patient in bed. He wa extremely feeble, much emaciated and markedly anæmic. Th skin of the face and limbs was of a dingy yellowish-brown hu The patient was naturally fair, the hair being of a light brow colour. The skin of the abdomen was very dark, resembling i colour the skin in a case of advanced Addison's disease more tha anything else. The areolæ of the nipples were dark. Severa flat moles were present on different parts of the surface of th body; the patient stated that they had existed since birth. Ther were no pigmented patches on the interior of the mouth. Th patient's brother stated that he had noticed that the patient's ski had been getting yellow and sallow for some time past. Th tongue and mucous membrane of the mouth were very dry; th tongue was slightly furred.

The temperature ranged from 99° to 100°, the pulse from 100 to 110. Dr. Menzies stated that it was always above 100. It was very small and extremely weak.

And here I must particularly note that at this visit neither Dr. Menzies nor I noticed any rigidity or thickening of the radial artery. This is certainly remarkable: for it is perhaps very difficult, I think I may say it is almost impossible, to believe that the rigidity and calcareous thickening, which were so marked on 1*st May* could have been developed in the course of a fortnight; and yet it is not likely that, if an advanced condition of rigidity and thickening had been present on 16*th April*, it could have escaped our notice, for at this date (April 16th) the pulse was so exceedingly small and feeble that it was only after very careful manipulation of the radial artery that the pulse wave could be felt.

The patient complained of pain and some tenderness in the lumbar region. He stated that his back had always been his weak point.

The heart's action was exceedingly feeble; the impulse imperceptible; the sounds almost inaudible. A soft blowing murmur was present both in the pulmonary and mitral areas.

There was no enlargement either of the liver or spleen.

The appetite was good and had been so throughout the whole course of the illness. The bowels were regular.

The skin was dry and somewhat harsh; the patient said that he seldom sweated. At the time of my visit, the axillæ were moist.

Blood.—The blood (examined on 18th April) showed a marked diminution of the red corpuscles; they numbered 2,700,000 per cubic millimetre. The white corpuscles were more numerous than normal, six or eight to each square; but there was nothing approaching leucocythæmia. The hæmoglobin was not estimated. The red corpuscles were quite natural in shape and size; the microscopic characters of the blood were in no way suggestive of pernicious anæmia. No pigment particles were detected in the specimen of blood which was examined.

Urine.—The urine was copious, measuring from three to three-and-a-half pints per diem; its specific gravity was 1010; the colour was very pale; it contained an appreciable but small quantity of albumin; it was loaded with phosphates. On microscopic examination, a few pus cells were detected in the scanty deposit. No tube casts were detected in the specimens of urine which were examined.

Cutaneous and subcutaneous tumours.—Hard, brawny swellings were present on:—(1) the anterior and posterior folds of each axillæ, especially on the anterior surface; (2) the flexor aspects of each elbow; (3) the upper part of each thigh, over the superior anterior processes of the iliac bones and over the adjacent parts of the inguinal folds; (4) the posterior fold of each buttock; and (5) in each popliteal space. (See Figs. 14 and 15.) The skin of the affected regions was of a purple-brown colour; it corresponded to the colour of the skin in lichen planus. The condition of the skin and subcutaneous tissues at the seat of the swellings more closely resembled a cancerous or sarcomatous infiltration than in any other condition which has come under my notice. But it was unlike any case of cancer or sarcoma which I have seen. The skin covering the subcutaneous swellings was rigid and thrown into folds. Many hard small nodules about the size of a small shot were situated in the margins of the swellings and in the adjacent skin. In the centre of the swellings the individual nodules seemed to have run together so as to form hard continuous masses.

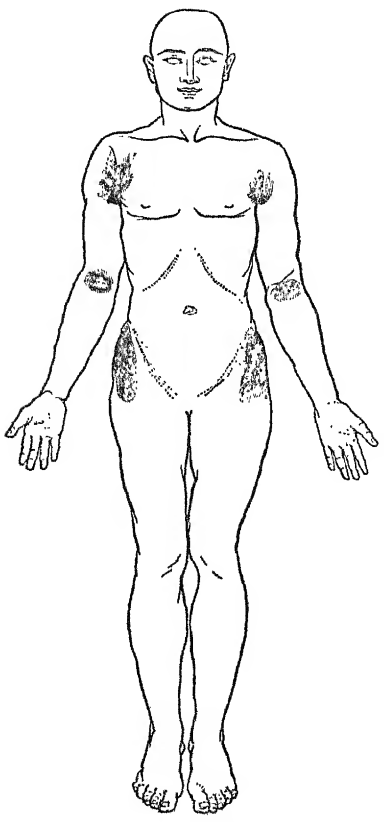


FIG. 14.—Diagram representing the position of the subcutaneous swellings in the case of calcareous degeneration described in the text. (Front view.)

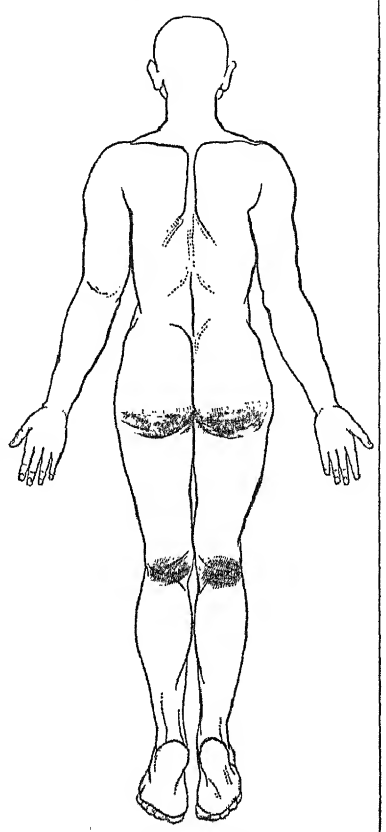


FIG. 15.—Diagram representing the position of the subcutaneous swellings in the case of calcareous degeneration described in the text. (Back view.)

The swellings were very hard and dense; in places they gave one the impression of being infiltrated with calcareous matter or with bone. This was especially evident in the flexor aspects of the elbows, where the subcutaneous infiltration and swelling were much less marked. In the bend of the left elbow, for example, the infiltration which in size was about the size of a florin, was quite superficial; it could be raised up by the fingers and gave one the impression of a thin, flat, bony or calcareous plate situated in the superficial layer of the skin.

Over the anterior spines of the iliac bones and adjacent parts, the affected areas of skin were of much larger size; the infiltrated areas in these situations both measured exactly $5 \times 3\frac{1}{2}$ inches.

The patient stated that the subcutaneous swellings were not painful; but some tenderness was complained of when they were firmly pressed upon.

When Dr. Menzies first saw the patient the knees were slightly swollen. At the time of my visit, several linear streaks were present in the skin covering the sides of the knees; they resembled the silvery bands on the abdomen which follow pregnancy; they looked as if the skin had been greatly stretched and the œdema had subsided and been absorbed.

The patient stated that standing on the feet was attended with some tenderness in the soles; but the skin of the soles looked perfectly normal in every respect.

There was no pain over any of the nerve trunks.

The optic discs were well defined; the fundus extremely pale; the pupils active both to light and accommodation.

So long as the patient was lying quietly in bed there were no cerebral symptoms; but the slightest effort, such as raising the head or sitting up in bed, was attended with giddiness and a feeling of faintness. The patient states that he has never had a headache during the whole course of his life.

Subsequent progress of the case.—The patient was again seen on 18th April. It was on this day that the blood was examined. On this day, too, a painting was made of the symmetrical swellings and the patient was photographed. The photographs were taken under difficulties, for the patient's bedroom was small and dark and he could not stand steadily even when supported, but one of them (reproduced in Plate XCIII. Fig. 9) was, considering the circumstances in which it was taken, successful. On raising him from the recumbent to the sitting position, he complained of giddiness and faintness; it was with the greatest difficulty that he managed, supported on each side, to walk two or three steps across the floor. We were glad to get him into bed again; his heart's action was so feeble that we were afraid he would die from syncope.

After this date, the asthenia rapidly increased.

1*st May.*—The patient was again seen in consultation with Dr. Menzies and the following note was made:—'He is much weaker and decidedly thinner. The skin is much darker. The subcutaneous swellings in the axillary, gluteal, and iliac regions are considerably larger; that on the right buttock is as large as an orange. There are many hard small colourless nodules about the size of small shot in the skin of the forearms, running down from the elbows.

'The tongue is furred and dry; the temperature is 100°·2; the pulsations of the heart number 108 to 120 per minute. During the past two or three days there has been some diarrhœa. The patient vomited last night without any obvious cause. Raising the head makes him feel very faint; he is consequently unable to sit up.

'Both radial arteries are absolutely rigid and pulseless; the hard rigid arterial cords can be easily traced from the wrists through the atrophied muscles of the forearms right up to the elbows. A very feeble pulsation can be felt in the brachial arteries. The femoral and popliteal arteries are rigid; it is with the greatest difficulty that any pulse can be felt in them. The heart sounds are even less distinct than they were at the last visit.'

On *5th May,* a to-and-fro (pericardial) friction sound was heard over the præcordium.

The patient died on 7th May. His mental condition was unclouded almost up to the very end.

Diagnosis.—The diagnosis presented very great difficulty; in fact, neither Dr. Menzies nor I were able to make up our minds as to the nature of the case; neither of us had ever seen anything at all resembling it.

The most striking features were:—The extreme asthenia and cardiac debility; the anæmia and emaciation; the rigid condition of the radial and superficial vessels; the pigmentation of the skin; the very remarkable symmetrical subcutaneous and skin swellings; and the character of the urine (copious, pale, low specific gravity, containing a large quantity of phosphates, a small quantity of albumin, some pus cells, but no tube casts).

The pigmentation of the skin and of the areolæ of the nipples and the profound asthenia and feeble action of the heart were suggestive of Addison's disease. In the final stages of Addison's disease exactly the same conditions may be present. But it was quite clear that the case was not a simple case of Addison's disease; the rigid condition of the radial and other superficial arteries and the remarkable subcutaneous tumours conclusively showed this.

The condition of the skin covering the subcutaneous swellings resembled a cancerous or sarcomatous infiltration, which had undergone, or was associated with, calcareous degeneration, more closely than anything else which had previously come under my notice; but if this view was correct, the remarkably symmetrical character of the malignant deposits was most peculiar. It is true that a few cases of symmetrical sarcoma of the skin have been recorded, but such cases are infinitely rare.

Nevertheless, I was disposed to think that some of the features of the case (the skin and subcutaneous lesions, the pigmentation and the asthenia) could be best explained by supposing that we had to deal with symmetrical malignant (sarcomatous or cancerous) deposits in the skin and malignant deposits in the suprarenal capsules

This view afforded no explanation of the rigid condition of the arteries, nor of the hard stone-like character of the subcutaneous infiltrations. Such a condition of arteries at the age of 25 has not, so far as I am aware, been recorded before.

Neither Dr. Menzies nor I attached any great importance to the condition of the urine. In this we were wrong, but the characters of the urine which I have described were in no way remarkable. The condition of the urine did not appear to any of us who saw the case to be a striking or prominent feature.

The age of the patient and the extremely feeble character of the heart's impulse, heart sounds and of the pulse seemed altogether opposed to the view that the patient was suffering from cirrhosis of the kidney. Further, there were from first to last no symptoms suggestive of uræmia, unless indeed the diarrhœa and vomiting, which occurred a day or two before death, were of this nature.

Post-mortem examination.—The post-mortem examination was made by myself at 9.30 on 8th May 1894. *Rigor mortis* was strongly marked. The infiltrated areas of skin and the subcutaneous swellings presented exactly the same appearances which they had had during life, with this exception that their colour was not quite so purple. All the subcutaneous swellings were removed.[1] To the naked eye they appeared to consist of dense firm inflammatory infiltrations; on section they cut 'gritty'; they were obviously infiltrated with calcareous matter.

The radial arteries were absolutely calcareous from top to bottom; the brachials were also calcareous, but less completely so. The iliac, femoral, popliteal and tibial arteries were completely calcareous; like the radials they were converted into hard rigid tubes. The renal arteries and many of the branches of the abdominal aorta were also infiltrated with calcareous material, though not so completely so as the radials, iliacs, femorals, etc.

The aorta throughout its whole extent was practically unaffected. The aortic coats were, in fact, thinner than normal and very elastic. Just above its bifurcation into the iliac arteries the coats of the abdominal aorta were infiltrated with calcareous material. The carotids were unaffected. The large vessels at the base of the brain and the small vessels throughout the brain were perfectly healthy.

The iliac, femoral, popliteal and radial arteries were partly filled with pale gelatinous clots; and in places with firm adherent ante-mortem thrombi.

The skin was of a dark, purple-brown colour; portions were removed for microscopical examination.

The muscles were for the most part healthy; some of the fibres of the gluteal muscles immediately adjacent to the subcutaneous swellings in the gluteal folds appeared to be calcareous.

The peripheral nerves seemed to be healthy.

One or two enlarged glands were present in the neck; one of them was removed for microscopical examination.

The pericardium contained about a couple of ounces of clear serum; both its visceral and parietal surfaces were covered with a thin layer of recent gelatinous lymph.

The heart was considerably enlarged; it weighed 1 lb. 2 ozs.; the increased size was almost entirely due to enlargement of the left ventricle.

The walls of the heart felt rigid. Immediately I took hold of the organ, and before the pericardium was opened, I said to Dr. Menzies that it was evidently infiltrated with calcareous material. On cutting into the heart, the cavity of the left ventricle remained widely patent; the walls of the organ did not collapse. The cavity measured $3\frac{1}{2} \times 1\frac{3}{4}$ in. The wall of the left ventricle at its thickest part measured $\frac{5}{8}$ths of an inch.

The interior of the left ventricle presented a very remarkable appearance; the papillary muscles and trabeculæ carniæ looked as if they were encrusted with calcareous matter. The appearance reminded me (in miniature) of the interior of a damp tunnel encrusted with lime salts. The shrinkage and decoloration produced by keeping the heart in spirit have almost entirely destroyed this appearance; but on running the finger over the interior of the left ventricle the calcareous encrustation can still be most distinctly felt. On section, numerous calcareous deposits were seen in the wall of the left ventricle. A few small calcareous deposits were also present in the walls of the right ventricle and of both auricles.

The valves were absolutely healthy.

The lungs, liver, spleen, stomach, pancreas and intestine were normal to the naked eye. The spleen was small and shrunken.

The right kidney could not at first be found. On tracing up the ureter, which was of normal size, the kidney was found to be represented by a thin firm mass of fibroid tissue; the kidney substance had entirely disappeared; there was practically no pelvis; the ureter was directly attached to this dense mass of fibrous tissue.

The left kidney was markedly contracted, very firm and dense. On section, it was found to be in an advanced condition of cirrhosis.

The right suprarenal capsule was perhaps a little larger than normal, but both suprarenal capsules were to the naked eye perfectly normal.

The brain was exceedingly anæmic. As I have already said, the arteries at the base were perfectly healthy and the small arteries throughout the brain were normal.

The pituitary body was slightly enlarged, and softer and paler than normal.

The thyroid gland was natural.

Portions of all the organs were immediately placed in Müller's fluid. Dr. Gulland kindly undertook the microscopical examination—a very laborious matter; and I am glad to take this opportunity of thanking him for the care and trouble and for the great amount of labour which he has expended on the case. The following is his report of the microscopical condition of the different organs and tissues:—

Microscopical Appearances (Dr. Gulland's Report). — The organs in this case were hardened in Müller's fluid and alcohol and cut in paraffin. The sections were stained on the slide in various ways, mainly with hæmatoxylin and eosin, and with the Ehrlich-Biondi mixture. What decalcification was necessary was done by the phloroglucin and nitric acid method.

Of the organs examined, the medulla, spinal cord, peripheral nerves, the liver, pancreas, suprarenal capsules, thyroid, pituitary body, lymphatic glands, and some of the arteries, were found to be normal.

In the *spleen* the only change of importance is the presence of an unusual quantity of a golden-brown pigment in the pulp. Some of this is to be found in the cell-bodies of leucocytes, but most of it is lying free in the spaces.

It is in the heart, in some of the arteries, in the kidneys, in the subcutaneous tumours, and in certain parts of the skin that the principal pathological changes are present.

[1] The subcutaneous swellings, the heart and other organs, with microscopical sections, were shown at a meeting of the Edinburgh Medico-Chirurgical Society (Feb. 5, 1896) at which this paper was read.

In the *heart* the muscular part of the wall alone is affected, and the change is a calcification of the individual muscle cells. The greater part of the heart wall is quite normal, but scattered through it are numerous islets of calcification. These calcified portions stain of a deep bluish purple in the hæmatoxylin and eosin specimens, and of a red purple in the sections stained with Ehrlich-Biondi. There is probably some kind of degeneration which precedes the calcification, but this cannot be distinguished from the calcification by its staining reactions. In the muscle-cell the degeneration commences in the cell-body, and affects the longitudinal and transverse fibrillation, which the purple staining renders very evident. Part of the cell only is affected at first, the rest, with the nucleus, remaining unaltered; sometimes the longitudinal fibrillation, sometimes the transverse, is first picked out. In the muscle-cells which are only slightly affected the calcareous matter is deposited in the form of minute granules in the lines of the striation. When the cell is fully calcified the structure ceases to be evident, but the gross shape is long retained. The very early stage is often found in isolated cells, but by the time a cell has become fully calcified, others around it have begun to share in the process. The calcified cells ultimately coalesce to form large irregular masses, of which the centre gives very little hint of its origin, the outer cells retain their shape, though their structure is lost, while the outermost cells of all often show the early stages of the process. (See Plate XCIII. Figs. 1, 2 and 3.)

The surroundings of these masses vary according to their size. The isolated calcifying cells lie in the midst of unaltered muscle. Round the larger masses the muscle-cells are often atrophied. As the calcareous masses enlarge, the intermuscular connective tissue round them becomes richer in nuclei, so that the calcified muscle-fibres are imbedded in a delicate connective tissue which is rich in nuclei. Here and there near the largest calcareous masses are to be seen a few giant-cells, of the kind which is better seen in the subcutaneous tumours.

Many of the *arteries* (such as the radials, iliacs, femorals, etc.) are completely calcified and converted into rigid tubes. All the coats are infiltrated and the structure completely obliterated.

Some of the arteries, which are least affected, show a calcification of the middle coat which will be described more fully in relation to the kidney, while in others the intima is thickened in patches. The internal elastic lamina is intact, but inside it there is a considerable amount of new connective tissue, well organised, and often six or eight times as thick as the normal intima. In this there are scattered very small calcareous nodules. The endothelium is everywhere intact.

The *kidney* shows alterations in the blood-vessels, the secreting parenchyma, and in the connective tissue. Of the vessels the arteries are most affected. In the renal arches, and in the larger arteries leading to them there is a calcification of the middle coat. The extra-nuclear part of the non-striped muscular fibres is first affected, though there is of course no picking out of the fibrillation as in the muscle-cells of the heart. The nucleus now ceases to be evident, but the shape of the calcified fibre is usually retained; it is only in some of the largest calcified patches that the structure of the middle coat is entirely lost and that a structureless tube takes its place. In many places the intima inside these calcified patches is replaced by the growth of a delicate œdematous connective tissue covered internally by endothelium. The lumen of the artery is often diminished to a quarter of its original size in this way.

In the interlobular arteries there is sometimes, though rarely, a calcified patch in the middle coat; the smaller arteries do not seem to be affected.

The glomeruli show the greatest variety of change. I cannot find one which is quite normal. Some of them are swollen and congested, and the epithelium covering them is desquamating. Others show every stage of inflammatory change, and a considerable proportion, especially near the surface of the organ, are represented by mere knots of fibrous tissue. In some of these latter, desquamation has gone so far that no nuclei are to be seen, whilst in others calcareous salts have begun to be deposited. The veins are apparently unaltered.

In the cortex all the tubes, except some of the collecting tubules, are in a state of catarrh. The capsular epithelium of almost all the Malpighian bodies is desquamating and degenerating; the epithelium of all the secreting tubules of whatever kind is either desquamating simply, or is degenerated in addition. In many of the tubules there are hyaline casts; some microscopic cysts with albuminous contents are to be seen here and there in the cortex.

The interstitial connective tissue is very greatly increased in amount, and is infiltrated with leucocytes to a considerable extent. Many of the lymphatic vessels are distended and full of leucocytes. The alterations in the kidney are represented in Plate XCIII. Figs. 4 and 5.

The calcified masses in the *skin* and in the *subcutaneous tumours* are disposed, at first sight, very irregularly, but they are found to be arranged mainly, if not entirely, in relation to the blood-vessels, especially the arteries. These are often to be seen, in the centres of the calcareous masses, completely calcified, and sometimes a tortuous calcified artery has been seen cut longitudinally for a considerable distance. (See Plate XCIII. Figs. 6 and 7.) From these arteries the calcareous material has evidently been poured out and has been deposited in the bundles of white fibrous tissue both in the corium and in the subcutaneous tissue.

In one section, part of the sheath of a nerve was calcified, but this seems to be exceptional. In the fibrous tissue the deposit takes the form of small granules, all nearly of the same size, lying close together, and being from 1 to 2 μ in diameter. These coalesce and the whole of the fibre on a transverse section becomes calcified; the outer part usually stains more deeply than the inner part and thus gives the impression of a tube. When a fibre is seen cut longitudinally it is rare to find the whole of it calcified equally. One part will be unaffected, another will be completely calcified and a third will show the early stage of granular deposition. The process results in the formation of irregular masses; the part first calcified is usually near the centre, as in the heart, whilst round the margin granules are often massed as though the change were spreading outwards. Of course collections of granules are often found in fibres at a distance from the larger masses.

The surroundings of the calcified masses vary very much as they do in the heart. The smaller ones lie in the normal connective tissue, especially in the skin, but the larger ones in the skin and almost all of them in the subcutaneous tumours are imbedded in connective tissue which gives more or less sign of reaction against the presence of the foreign material. This tissue is looser, contains a fair number of leucocytes, though not any great amount of infiltration, and contains specially a very large number of giant-cells, in every stage of development from ordinary leucocytes upwards. (See Plate XCIII. Fig. 8.) The fully formed cells are multinucleated, and closely resemble the giant-cells seen in tubercles, or those known as osteoclasts, which are concerned in the removal of bone. Like the latter, too, these giant-cells are closely apposed to the calcareous masses, and they often lie in depressions on the surface. There can be little doubt that they represent an attempt on the part of the tissues to remove the calcified material. They are far more abundant in the subcutaneous tumours than in the skin.

Remarks.—From the foregoing account of the post-mortem appearances and from Dr. Gulland's report, it will be seen that the most striking features are:—

1. *The condition of the heart.*—The organ is an extraordinarily fine example of calcareous degeneration. Numerous calcareous deposits are distributed throughout the walls of the organ, more especially in the wall of the left ventricle. The trabeculæ carniæ and papillary muscles of the left ventricle are almost entirely calcified. The calcareous infiltration affects not only the interstitial tissue, but the muscular fibres of the heart. The calcareous infiltration of the muscular fibres is admirably seen both in transverse and longitudinal sections. (See Plate XCIII. Figs. 2 and 3.)

2. *The condition of the arteries.*—I have not been able to find or hear of any case in which such an extraordinary calcareous infiltration of the blood-vessels as was present in this case was developed in a young person. The iliac, femoral, popliteal, tibial and radial arteries were absolutely calcareous from top to bottom and converted into rigid tubes.

3. *The subcutaneous tumours.*—Many of the arteries in the subcutaneous tissue and deeper layers of the skin were calcareous, and numerous calcareous deposits were present in the subcutaneous tissues. The calcareous material was in some places deposited in wavy lines which evidently represented the course of blood-vessels and arteries. (See Plate XCIII. Fig. 6.) It is certain, I think, from the microscopical appearance which the subcutaneous swellings present that the calcareous material had been infiltrated around the blood-vessels and that this infiltration had led to the production of inflammatory changes in the connective tissue and to the production of the giant-cells, which Dr. Gulland has described. (See Plate XIII. Fig. 8.)

4. *The condition of the kidneys.*—The right kidney was entirely destroyed, evidently as the result of old disease. This in all probability had occurred during the severe (six months) illness which occurred when the patient was eleven years of age.

The left kidney was in a condition of very advanced cirrhosis. Many minute calcareous deposits were present in the cortex; the arteries in the pyramidal portion were calcareous. It is obvious that an advanced condition of cirrhosis must have been present for many months before the patient's death. Now, considering that one kidney was entirely destroyed and that the other was so markedly cirrhotic, the absence of any definite symptoms of kidney disease and of any uræmic symptoms is very remarkable.

Theory as to the pathological course of the case.—Putting all of the facts together, it seems to me that the most probable explanation which can be advanced of this extraordinary case is the following:—(1) That in early life (at the age of eleven) the patient suffered from pyelonephritis of the right kidney; that the right kidney had at this time been entirely destroyed; (2) That the exposure and hardships to which he had been subjected in America eighteen months before his death had induced disease in the other kidney, or, what is perhaps more probable, had aggravated a cirrhotic process which was already present in the left kidney, and that this had slowly and gradually progressed until the extreme condition of cirrhosis which was found after death had been produced; (3) That, for some reason or another which I cannot explain, the blood had become impregnated with calcareous salts in solution; (4) That owing to the advanced cirrhotic condition of the kidney, the calcareous material had (instead of being excreted by the kidney) been retained in the blood and finally deposited in the walls of the heart and peripheral arteries, and extravasated into the subcutaneous tissues; and (5) That local irritation, the result of mechanical movement, probably played a part in determining the deposit of the calcareous material in the walls of the heart and in the subcutaneous tissues over the joint surfaces, gluteal and axillary folds, etc.

The localisation and symmetrical distribution of the skin and subcutaneous lesions can only, I think, be accounted for by supposing that some mechanical condition or conditions (such as movement and stretching) was concerned in their production.

The following reasons seem to suggest that the calcareous infiltration of the heart, arteries and subcutaneous tissues, was rapidly produced:—(a) It is difficult to conceive that the heart and arteries could have been affected in any marked degree with calcareous degeneration when the patient first went to Glasgow three months before his death. He stated that for some weeks after going to Glasgow he was able to engage without any shortness of breath or discomfort, in hard laborious work. It is hardly possible to believe that with such a condition of heart and arteries as was present at the time of death, the patient could have been equal to any prolonged and violent muscular effort.

(b) It seems certain, both from his own statement and from the statement of Dr. Menzies, that the subcutaneous swellings were not present, when he came from Glasgow some six weeks before his death.

After this time, the asthenia rapidly increased, and when I first saw the patient it was with the greatest difficulty that he was enabled to stand in the erect position and walk a few steps across the floor to get into a chair to be photographed. It seems probable that for some reason or other the blood became loaded with calcareous material some six or eight weeks before his death, and that it was after the strain of the back that rapid calcareous infiltration in the heart and arteries took place.

It is curious, considering the feeble character of the pulse and the careful manipulation which was required to detect the pulse wave, that the rigid condition of the radial artery was not observed at the time of our first consultation, a fortnight before the patient's death; for, as I have already stated, it is almost impossible to believe that the extreme degree of calcareous infiltration which was present at the time of death could have been developed in the course of a few days. It must however be admitted that the calcareous subcutaneous swellings, and probably therefore the calcareous deposits in the skin, were developed in the course of a few weeks.

In describing the clinical course of the case I have pointed out that in some of its features—notably the pigmentation of the skin, the extreme feebleness of the heart's action, the marked asthenia and the apparently causeless diarrhœa and vomiting—it closely resembled a case of Addison's disease. I may add that I have met with some other cases of cirrhosis of the kidney in which the same difficulty of diagnosis occurred.

DESCRIPTION OF PLATE XCIII.

Fig. 1.—Transverse section through the wall of the left ventricle in the case of calcareous degeneration described in the text, showing calcareous transformation of the muscular fibres of the heart. (Very low power.)

The letter P, points to the pericardial surface; the letter E, to the endocardial surface. The section is made through the whole thickness of the wall of the left ventricle. a, a, groups of muscular fibres which have undergone the calcareous degeneration.

Fig. 2.—Longitudinal section through the muscular fibres of the heart in the case of calcareous degeneration described in the text. (High power.)

The letter a, points to normal muscular fibres longitudinally divided; b, b, to muscular fibres in which the calcareous degeneration is just commencing; c, c, to fibres which are markedly affected with calcareous degeneration; d, to longitudinally divided fibres which are enormously swollen and completely calcareous.

Fig. 3.—Transverse section through the wall of the left ventricle in the case of calcareous degeneration described in the text, showing the calcareous transformation of the individual muscle fibres. (High power.)

The letter a, points to normal muscular fibres of the heart transversely divided; b, to normal muscular fibres longitudinally divided; c, c, to calcareous masses, the remains of degenerated muscular fibres seen in transverse section; d, to fine fibrillated connective tissue surrounding the fibres which are affected with calcareous degeneration.

Fig. 4.—Transverse section through the cortex of the kidney in the case of calcareous degeneration described in the text. (Low power.)

The letter A, points to the capsule; B, to a Malpighian body containing calcareous material; C, to a tubule containing a hyaline cast. A densely nucleated connective tissue is seen to be present between the tubules.

Fig. 5.—Section through the kidney in the case of calcareous degeneration described in the text. (High power.)

The large calcareous mass (C) is seen lying in the midst of the cirrhosed kidney substance; D, the cirrhotic tissue.

Fig. 6.—Section through a portion of one of the subcutaneous tumours in the case of calcareous degeneration described in the text, showing the calcification extending along the lines of the arteries. (Magnified $3\frac{1}{2}$ times.)

The letters a, a, point to a dense mass of calcareous material in the superficial portion of the section; b, b, b, to minute calcified vessels passing from the subcutaneous tissue into the subjacent muscles. The muscular fibres are seen to be transversely divided.

Fig. 7.—Section through the skin and subcutaneous tissues in the case of calcareous degeneration described in the text. (Low power.)

The letter A, points to the free surface of the skin; B, to transversely divided arteries, the walls of which are thickened and partly calcified; C, to large mass of calcareous material in the subcutaneous tissue.

Fig. 8.—Section through a portion of one of the subcutaneous swellings in the case of calcareous degeneration described in the text, showing dense calcareous infiltration and giant-cells. (High power.)

The letters A and C, point to the dense calcareous masses; B, to giant-cells lying in the midst of a richly nucleated connective tissue.

Fig. 9.—Photograph showing the subcutaneous swellings in the axillæ and bends of the elbows.

CHLOROSIS

THIS disease, to which the synonym 'green sickness' is sometimes applied, is by far the most common form of primary anæmia. It varies very greatly in severity in different cases. It is characterised by all the typical symptoms of anæmia—pallor, shortness of breath, palpitation, giddiness, etc. The essential blood change is a deficiency of hæmoglobin; in the great majority of cases the red blood cells are comparatively little diminished in number, but the richness of the individual red blood corpuscles in hæmoglobin as well as the total amount of hæmoglobin in the blood are markedly below the normal.

Etiology.—Chlorosis is essentially a disease of the female, and in the vast majority of cases is developed at or about the time of puberty. Cases which appear to be closely allied to chlorosis are occasionally, but very rarely, met with in males. Children, too, are occasionally affected.

In the great majority of cases, the disease develops between the ages of 15 and 25; but cases of apparently causeless anæmia, in which the blood presents all the characters of chlorosis and which are curable by iron, are sometimes met with in older women.

The disease occurs amongst all classes of society, but in my experience it is most common in young servant-girls. Want of fresh air and sunlight undoubtedly seem to predispose to its production. It is more common in towns than in the country. Country girls who come into service in town are particularly apt to be affected.

The exact causation of chlorosis has given rise to a great deal of difference of opinion.

It used to be thought that the disease was due to disappointment in love; and there can be no doubt that mental anxiety or grief may act as contributory or exciting causes, but only perhaps in persons predisposed to chlorosis or already suffering from it.

Derangement or disease of the uterus and ovaries has been suggested as a cause. Amenorrhœa is usually present in chlorosis, but it appears to be the result, not the cause, of the disease. Proof of this is found in the fact that in some well-marked cases of chlorosis the menstruation is perfectly regular and natural in every respect. In the great majority of cases of chlorosis in which the menstruation is regular in time the discharge is deficient in quantity and too pale in colour.

But although amenorrhœa is not the cause of chlorosis, there can, I think, be little doubt that the active strain which is thrown upon the tissues and organs of the female at the time of puberty is an important factor in the production of the disease. According to Niemeyer, chlorosis is invariably developed in girls who begin to menstruate before the mammæ and genital organs are developed. My own view is that the unusual strain, so to speak, which is thrown upon the blood-forming organs by the rapid development of the tissues and organs which occurs at the time of puberty, and especially by the development of the function of menstruation, is a most important factor in the production of the condition. This view seems to me to be supported by the fact that as the patient gets older (in other words, as the organism becomes accustomed to the strain on the blood-forming organs which menstruation entails) the disease and the tendency to relapse which is such a striking feature of it gradually disappear.

Virchow thought that chlorosis was due to defective development of the aorta and arterial system; but narrowing of the aorta and thinness of the arterial coats are probably the result and not the cause of the condition; or perhaps it would be more correct to say that the two conditions (*a*, narrowing of the aorta and thinness of the arteries; and *b*, chlorosis) are the result of a common cause, the defective development of the aorta and arterial system being perhaps due to a congenital condition.

Sir Andrew Clark supposed that chlorosis was the result of auto-intoxication from the intestine due to constipation. Constipation is certainly very common in cases of chlorosis, but it is by no means always present. In quite a number of well-marked cases which have come under my own observation, more especially amongst girls belonging to the upper orders of society, constipation has been entirely absent. In some of these cases, I have satisfied myself that the bowels were not only opened, but sufficiently freely opened, every day. It must, however, be remembered that auto-intoxication from the intestine may probably occur even when there is no constipation; and I am willing to grant that constipation and auto-intoxication from the intestine may have some influence in the production of the disease, but in my opinion they are not the essential and fundamental causes.

Deficiency of hydrochloric acid in the gastric juice, ulceration of the stomach and gastric hæmorrhage have been suggested as the cause of the disease. Possibly these conditions may in some cases act as predisposing causes; but in most cases they are in my opinion results rather than the cause of the disease. Tight-lacing has also been blamed.

As I have already stated, the essential clinical feature of chlorosis is a diminution of the hæmoglobin—a deficiency of the iron of the blood. Further, in order to understand the causation of the disease it must be remembered:—(a) that chlorosis is essentially a disease of the female sex; (b) that it is in the vast majority of cases developed at or about the period of active sexual development; and (c) that it is speedily and easily cured by the administration of iron—provided only that the iron is given in sufficiently large quantities and that the gastro-intestinal tract is in a sufficiently healthy state to permit of the absorption of the remedy.

The essential causes of chlorosis, then, would appear to be:—(1) a functional derangement of the gastro-intestinal tract which prevents the absorption of the iron of the food, or which splits up the soluble iron compounds and renders them

unfit for absorption into the blood; and (2) the strain which is put upon the blood-forming organs of the female by the rapid development which takes place at or about the time of puberty, and especially perhaps by the unusual strain which the development and establishment of the function of menstruation entail.

Clinical History.—The onset of the disease is insidious. The patient gradually loses colour, complains of debility and inability for exercise, becomes short of breath, and suffers from palpitation and giddiness—in short, the disease is characterised by the presence of symptoms which are associated with a deficiency of hæmoglobin in the blood, and which result from the fatty and dilated condition of the heart which the deficiency of hæmoglobin and the consequent imperfect oxygenation of the heart muscle occasion.

The essential features in the pathological physiology of chlorosis may be summed up in a few words, namely, deficiency of hæmoglobin, fatty degeneration of the heart muscle and of the other tissues and organs, a condition of irritable weakness of the heart, cardiac dilatation, and the results of these conditions.

Patients who are affected with a high degree of chlorosis are, as a rule, well covered with fat, but their muscles are usually soft and flabby. In many cases, the mammæ are full, the external genitals and the pubic hair well developed; but in other cases this is not so. In those cases in which dyspepsia or ulceration of the stomach is associated with the anæmia, some emaciation may be present.

The skin and mucous membranes are pale, and the skin often has a greenish-yellow colour; hence the term 'green sickness' which has been given to the disease. The green hue is more marked in girls of a dark complexion. In blondes, the complexion often has a beautiful rosy-red tint when the patient first comes under the notice of the physician; patients suffering from chlorosis flush readily; their complexions are naturally delicate and the temporary tinting of the skin which results from the flushing is very becoming, for many of the girls who are affected with chlorosis are very pretty. After the temporary excitement subsides, the face becomes pale; and in severe cases both the lips and skin may look almost entirely bloodless. Pallor of the buccal mucous membrane and conjunctiva is, from a diagnostic point of view, of more importance than pallor of the skin.

Patients affected with chlorosis complain of shortness of breath on exertion, palpitation, giddiness on stooping the head and on suddenly rising from the recumbent to the erect position, debility, inability for prolonged and sustained efforts either of body or mind. In advanced stages of the disease, the feet and legs may be œdematous. The nails are in many cases thin and misshaped.

The symptoms are so characteristic and constant that in well-marked cases of chlorosis it is possible to predict most of the symptoms which are present when the patient comes under observation and before a single question has been asked. Further, since the administration of Blaud's pills is the ordinary routine plan of treatment, one can in many cases predict that the patient has been taking three pills three times a day.

Dyspeptic derangements are very common; loss of appetite or a capricious appetite is usually present. In some cases there is flatulent dyspepsia with pain some time after eating; in these cases, the dyspepsia is usually the result of the anæmic condition of the stomach and intestine and of the impairment of the digestive power which results therefrom. In other cases, ulceration of the stomach is present. Chlorosis and simple perforating ulcer of the stomach are often seen in combination. I do not of course mean to say that most chlorotics are the subjects of ulceration of the stomach, but that in a large proportion of cases of ulcer of the stomach the patients are chlorotic. The anæmic condition of the gastric mucous membrane undoubtedly predisposes to the production of the ulcer.

In many cases of chlorosis, the tongue is pale, flabby, indented by the teeth and slightly furred; in others, it is pale and clean. Constipation is very usually present, but is not an essential or invariable symptom. There is usually some utero-ovarian derangement, generally amenorrhœa. This, as I have already stated, is probably the result and not the cause of the disease. As I have already pointed out, in exceptional cases of chlorosis the menstruation is perfectly regular in time, though in cases of this kind it is usually pale and scanty in amount. In many cases of chlorosis there is leucorrhœa, doubtless the result of the enfeebled tone, both general and local.

Nervous symptoms, such as giddiness, which is of course due to defective blood supply to the brain, tinnitus, headache and neuralgia are often complained of. The late Dr. Anstie used to say that neuralgia was a prayer on the part of the nerves for a better supply of blood. In many cases the temper is irritable and uncertain. Hysterical symptoms are of frequent occurrence. Sleeplessness is comparatively common. Fainting may occur after slight effort, such for example as suddenly rising from the recumbent to the erect position, after a watery evacuation of the bowels, etc.

Hæmorrhages of any considerable amount are exceedingly rare, except in those cases in which hæmatemesis results from associated ulceration of the stomach; in cases of this kind, the hæmorrhage is, as I have already pointed out, an indirect, not a direct, result of the disease. When profuse it may of course materially aggravate the condition.

In a small proportion of cases of chlorosis, optic neuritis occurs. It is especially apt to be developed in those cases in which there is hypermetropia; and since patients affected with chlorosis frequently suffer from headache, the combination of headache with double optic neuritis may lead the physician to suppose that he has to deal with the presence of a cerebral tumour.

The condition of the heart and pulse in cases of chlorosis is very important. As I have already stated, palpitation is a frequent symptom; it is due to the condition of irritable weakness of the heart muscle. Slight excitements whether of body or mind produce an unusual effect upon the irritable heart. The pulse is readily excited. In the earlier stages of the disease, the pulse tension is usually good, in fact it may be high; but when the chlorosis is long-continued or severe, the pulse tension is in my experience almost invariably low. Sphygmographic tracings often show the undue irritability of the heart in a striking way.

When the patient is perfectly tranquil and at rest the cardiac impulse is usually feeble and diffuse; under excitement the apex beat becomes much more forcible and well defined; the apex beat is usually displaced somewhat downwards and outwards to the left; the cardiac dulness is increased both to the right and to the left. The ventricles, particularly the left ventricle, are usually more or less dilated. On

auscultation, a systolic murmur is usually present in the pulmonary and often in the mitral and tricuspid areas. Occasionally a systolic murmur is also audible in the aortic area. The mitral and tricuspid murmurs are of course due to regurgitation, the result of muscular and relative incompetence. The exact mode of production of the pulmonary and aortic murmurs is more difficult to explain; they appear to be due partly to the altered condition of the blood, partly to the altered relationship of the pulmonary orifice to the pulmonary artery, and partly to the altered mode of contraction of the heart. In cases of chlorosis the pulmonary artery is usually somewhat dilated and the action of the heart is, at all events under excitement, quick and the contraction of the cardiac muscle rapid and sudden. The sudden propulsion of a large wave of hydræmic blood into the pulmonary artery which is, in comparison to the orifice, relatively dilated, seems to me the most reasonable explanation of the mode of production of the pulmonary murmur. I am quite unable to accept Dr. George Balfour's theory that the murmur is a systolic mitral murmur propagated to the pulmonary area through the appendix of the left auricle, which he states comes to the surface and overlaps the pulmonary artery in the 2nd left interspace. I need not discuss the question in detail, for I have considered it at considerable length in my work on the heart. I need only repeat that Dr. Balfour's theory seems contradicted by the facts that in many cases of chlorosis there is no mitral murmur but only a pulmonary murmur, and that in cases of profound anæmia which prove fatal (cases of pernicious anæmia, for example, in which the same pulmonary murmur is present), the appendix of the left auricle, as Dr. William Russell was the first to point out and as my pathological experience abundantly confirms, rarely if ever overlaps the pulmonary artery. Owing to the dilation of the right heart and the twisting of the organ on itself which results therefrom, the left auricular appendix is usually entirely concealed by the pulmonary artery and does not come to the surface of the chest at all.

Some authorities state that in some cases of chlorosis a diastolic aortic murmur is occasionally also present; but I doubt the correctness of this opinion. I agree with Dr. Sansom in thinking that what appears to be the diastolic portion of a double aortic murmur is probably the venous murmur in the neck heard at the aortic orifice during the diastole of the heart.

In many cases of profound chlorosis the veins of the neck are dilated. A flickering pulsation can not unfrequently be observed in the dilated external jugular vein on careful observation. In those cases in which a considerable degree of tricuspid regurgitation is present, true venous pulsation in the external jugulars may be well marked.

The condition of the blood is of the greatest importance. In slight cases, the red blood corpuscles are little if at all diminished in number. In severe cases, they usually number from 2,500,000 to 3,500,000 per cubic millimetre. In very exceptional cases they are much more reduced. Hayem has reported a case of chlorosis in which the blood corpuscles numbered only 1,300,000; but such a marked decrease in the red blood corpuscles is altogether exceptional.

The essential blood change is a diminution in the hæmoglobin. As estimated by Gowers' instrument, which in my experience reads low, the hæmoglobin may be reduced to 30, 25, or even 20 per cent. The individual richness of the red blood corpuscles in hæmoglobin is in many cases less than half the normal—for example, $\frac{H}{R.C.}=\frac{30}{66}$.

In many cases, the red blood corpuscles present little or no alteration either in size or shape; a few large red corpuscles are not unfrequently present, but microcytes are in my experience exceedingly rare. The extreme alterations in the size and shape of the red blood corpuscles which are so characteristic of pernicious anæmia are very rarely present. In such cases of chlorosis as that described by Hayem in which the number of the red blood corpuscles was reduced to 1,300,000 —in which in other words a very rapid production of red blood corpuscles is demanded—one would naturally expect that the red blood cells (in consequence of the extraordinary demand made upon the blood-forming organs) would be imperfectly formed and consequently altered in size and shape as they are in pernicious anæmia. But the extreme alterations in size and shape of the red blood corpuscles which are so common in cases of pernicious anæmia, have not been present in any case of chlorosis which has come under my own notice.[1]

The blood platelettes are usually normal. The white blood corpuscles are not increased in number.

The urine rarely presents any characteristic change. In my experience, it is generally pale and of low specific gravity, but free from any abnormal constituents.

In some cases, febrile symptoms are developed. A slight degree of pyrexia may be the result of some agitation or excitement; a decided degree of pyrexia is usually due to the development of venous thrombosis or some other accidental complication. Anæmic fever properly so-called, such as is frequently seen in cases of pernicious anæmia, is exceedingly rare.

Venous thromboses occasionally occur. In my experience, they are much more frequent than some writers have stated. The veins of the calf are usually affected. The clot not unfrequently extends up to the femoral vein. The onset is usually sudden. The patient complains of pain in the calf, which becomes considerably swollen, hard and exceedingly tender; the foot and ankle swell; there is often at the same time a very marked elevation of temperature. In rare cases, the condition is bilateral, one vein being first affected and the corresponding vein on the opposite side after an interval of time becoming involved. In very rare cases, the venous sinuses within the cranium may become thrombosed, or a portion of clot which has been detached from the femoral veins may be swept through the circulation and may produce fatal plugging of the pulmonary artery. No cases of this kind have come under my own observation.

Diagnosis.—The diagnosis of chlorosis rarely presents any difficulty. The condition is obviously a primary anæmia. There is rarely any suspicion of associated disease unless the stomach happens to be seriously deranged.

The Differential Diagnosis of Chlorosis and of Dyspepsia and Ulceration of the Stomach.—In cases in which dyspeptic symptoms are associated with chlorosis, the stomach symptoms may, as I have already stated, be the result either of anæmic changes with loss of functional activity in the walls of the stomach, or of ulceration. In those cases in which hæmatemesis occurs and in which the patient comes under observation

[1] Alterations in the shape of the red blood corpuscles may, it must be remembered, be due to want of due care and precaution in preparing the microscopical preparation.

for the first time after the occurrence of the bleeding, it is important to determine whether the patient was bloodless before the hæmatemesis, or whether the anæmia is the result of the bleeding.

The Differential Diagnosis of Chlorosis and Phthisis.—In some cases of phthisis, there is a considerable degree of anæmia at the onset of the disease; but these cases are not likely to be mistaken for chlorosis by a careful and competent observer; they are attended with definite symptoms and physical signs indicative of the lung disease.

The Differential Diagnosis of Chlorosis and of Bright's disease.—Bright's disease may also be mistaken for chlorosis by a careless observer. The condition of the urine at once shows the true nature of the case

The Differential Diagnosis of Chlorosis and of Lead poisoning.—In some cases of lead poisoning a profound degree of anæmia is present, and if, as is often the case, the patient should happen to be a young woman the case may easily be mistaken for chlorosis. In both conditions, constipation and amenorrhœa are usually present. The presence of a blue line on the gums, the fact that the patient has been exposed to lead poisoning, the occupation of the patient and the presence of other symptoms suggestive of plumbism (such as dry colic, rheumatism, wrist-drop, etc.) are usually sufficiently distinctive of the true nature of the condition.

The Differential Diagnosis of Chlorosis and of Chronic Mitral disease.—The differential diagnosis of a primary cardiac lesion and of the chlorotic heart is not always easy. In the earlier stages of chlorosis in which a pulmonary systolic murmur is alone present, there is of course no difficulty. It is in the advanced stages when the heart cavities become dilated, when murmurs are developed at the mitral and tricuspid orifices that the chief difficulty of diagnosis occurs. In cases of this kind, the patient suffers from palpitation and shortness of breath, and œdema of the feet may be present. The condition may consequently be easily mistaken by an inexperienced observer for a case of primary heart disease. But the profound anæmia and the condition of the blood (the marked deficiency of hæmoglobin) at once suggest the true nature of the case. It is only in those cases in which there is a history of previous rheumatism, or where there is reason to suppose that the heart was affected before the bloodless condition developed, that the diagnosis presents any real difficulty.

In doubtful cases, the effects of treatment are most important in deciding the true nature of the condition. Chlorosis is, as I have already stated, easily cured by appropriate treatment, and with the disappearance of the anæmia, the heart symptoms and physical signs subside and gradually disappear. With the supply of iron to the blood, the heart muscle recovers its tone, and the fatty changes disappear. It must be remembered that while in some cases fatty degeneration is a very grave disease, in others, as in chlorosis, it is eminently curable. It cannot be too forcibly insisted on that the prognosis in cases of fatty heart depends entirely upon the cause of the condition—whether that cause is removable by treatment or not.

The Differential Diagnosis of Chlorosis and Ulcerative Endocarditis.—This rarely presents any difficulty, although the two conditions are, as regards some of their symptoms, very similar. In both diseases, a profound condition of anæmia, a greenish-yellow or lemon-yellow tint of the skin, cardiac murmurs, a dilated and unduly irritable condition of the heart, with arterial murmurs, a jerking visible condition of the pulse and a distended and pulsating condition of the veins in the neck may be present. In ulcerative endocarditis there is usually more or less fever, and some cases of chlorosis are, as I have already stated, attended with slight and temporary pyrexia.

The chief points of distinction are:—the age and sex of the patient; the condition of the blood; the character of the febrile disturbance; the condition of the spleen; and the presence or absence of symptoms indicative of embolic infarction.

Chlorosis is, as we have seen, essentially a disease of young women. Ulcerative endocarditis may, of course, occur at the same age, but it is comparatively speaking uncommon in young women. The sex of the patient and the age of the patient are consequently of some importance.

In chlorosis, the anæmia, and especially a deficiency of hæmoglobin, are the fundamental features of the case, while the altered condition of the heart is secondary. But in ulcerative endocarditis, the anæmia is secondary to and the result of the cardiac lesion. The history of the case and the way in which the anæmia has developed are consequently of importance for the purposes of diagnosis.

In chlorosis, fever is rare except as a mere temporary occurrence, or as the result of some well-marked complication such as thrombosis of the veins of the leg; while in ulcerative endocarditis, fever is almost always present and is a striking feature of the case

In ulcerative endocarditis, the spleen is usually enlarged and symptoms indicative of embolic infarctions and of peripheral inflammations, the result of minute infarctions, are often developed.

Further, in cases of ulcerative endocarditis, it is obvious that the patient is seriously ill; the general condition is suggestive and indicative of danger. This is rarely the case in chlorosis, although in any profound condition of anæmia, the patient may look extremely ill and manifest great exhaustion after effort. I recently had in hospital a case in point—a profound case of chlorosis—in which the patient walked up to the hospital. On admission, her condition was suggestive of great danger, but a few days' rest in bed and appropriate treatment were immediately followed by improvement and a striking change in the appearance of the case.

Lastly, and this is a most important point, the effects of treatment are of the greatest diagnostic value.

The Differential Diagnosis of Chlorosis and Pernicious Anæmia.—When the observer has satisfied himself that the anæmia is primary, that there is no obvious disease in any of the organs to account for it, and that the bloodlessness is the chief clinical characteristic of the case, the question arises whether the case is one of chlorosis or of pernicious anæmia. In the great majority of cases there is no difficulty in deciding this point.

The chief points to which attention should be directed in order to decide the question are:—(1) *The age and sex of the patient.* Pernicious anæmia rarely occurs in young women, while chlorosis is almost exclusively a disease of young women.

(2) *The condition of the blood.*—In pernicious anæmia, the red blood corpuscles are enormously reduced in number; though the total amount of hæmoglobin is often markedly diminished, the richness in hæmoglobin of the individual red blood corpuscles is usually equal to, or even above, the normal; the red blood corpuscles do not form rouleaux, and they present marked variations in size and shape. Whereas, in chlorosis the red blood corpuscles may be almost up to the normal

average number; while the total hæmoglobin is not only decreased but the richness in hæmoglobin of the individual red blood corpuscles is markedly below the normal; and apart from the pallor of the red blood corpuscles the microscopical characters of the blood usually present little or no difference from the normal. The extreme variations in size and shape which are so characteristic of pernicious anæmia are very rarely present.

(3) *The therapeutic effect of iron*.—In pernicious anæmia, iron usually produces no improvement, in fact in many cases it seems to make the patient worse; while in chlorosis, rapid improvement follows the administration of iron, provided always that the iron is given in sufficiently large doses and that the gastro-intestinal tract is in a healthy condition.

(4) *The presence of pyrexia*.—In chlorosis, febrile disturbance is rarely developed except as the result of some intercurrent complication such as thrombosis of the veins of the leg; whereas, in pernicious anæmia, intercurrent and apparently causeless attacks of pyrexia (true anæmic fever) are of frequent occurrence and of considerable diagnostic value.

(5) *The condition of the urine*.—This is, in my experience, an uncertain diagnostic, though Dr. William Hunter attaches much importance to it. In chlorosis, the urine is usually paler than normal. In pernicious anæmia, the urine may be of normal colour or pale, but is apt from time to time (during the temporary exacerbations) to be darker than normal.

Prognosis.—In cases of chlorosis the prognosis is eminently favourable, unless the disease should happen to be attended with some grave complication, such as ulcer of the stomach, thrombosis of the cerebral sinuses, etc. There are few diseases which are more amenable to treatment than chlorosis. Nevertheless, a marked degree of chlorosis should never be made light of; for so long as the profound anæmia continues, complications of a serious kind are apt to be developed. I have already referred to the frequency with which ulceration of the stomach is developed in cases of chlorosis; consequently the possibility of the occurrence of this serious complication should always be kept in view. Further, in a certain proportion of cases of chlorosis, thrombosis of the veins is developed. When the veins of the leg are affected, the condition is usually recovered from; but in rare cases the cerebral veins may become thrombosed, or a portion of clot from the thrombosis may be detached from the femoral vein and may be swept through the circulation with the production of fatal plugging of the pulmonary artery. Again, the development of an acute disease in the course of chlorosis, such, for example, as influenza or acute croupous pneumonia, is always a serious matter. An example in point recently occurred in my hospital practice. A young woman who, for several months, had suffered from profound chlorosis, was admitted suffering from an attack of acute croupous pneumonia. Although the lung lesion was only moderate in extent, the patient died notwithstanding the assiduous administration of oxygen inhalations, hypodermic injections of strychnine, free stimulation, etc. The fatal issue was, I believe, entirely due to the chlorotic condition of the heart. In acute croupous pneumonia, the prognosis, as every one knows, largely turns upon the condition of the heart. The fatty and dilated heart of chlorosis is quite unable to stand the strain of a severe attack of continued fever or of a severe attack of acute croupous pneumonia.

For the reasons just stated, it will be apparent that it is eminently desirable to cure cases of chlorosis as speedily as possible, and so long as the chlorotic condition continues to guard the patient carefully from exposure to the causes of acute febrile disease and from conditions likely to produce intercurrent complications.

Treatment.—In the treatment of chlorosis, the essential point is to supply iron to the blood. I will presently refer to the method which in my experience is most effectual for this purpose. But before doing so, let me say a word or two with regard to the general management and hygienic treatment.

In all cases in which the bloodlessness is marked, it is, in my opinion, of great importance to keep the patient at rest in bed. One reason why the disease is so much more easily cured in hospital than in private practice is, I think, because the hospital patients are kept in bed. The absolute rest in the recumbent position removes all strain from the heart (a most important point) and aids the recuperative powers. In chlorosis anything which excites the body or mind and which is apt to suddenly accelerate the heart's action should be avoided.

While the patient is lying in bed, her surroundings should be as bright and pleasant as possible. It is very desirable that she should have plenty of fresh air and an abundance of sunlight when it can be obtained There can, I think, be no question that sunlight hastens the cure.

The temperature of the bedroom should be kept between 55° to 60°, rather on the cool than on the hot side

The food should be nutritious and easily digestible. When there are no dyspeptic symptoms, an ordinary mixed diet, consisting of milk, milk foods, fish, white meat, butcher meat, a moderate amount of vegetables, and fruit, may be allowed. Oranges and lemons are usually grateful to chlorotic patients; they often seem to have a craving for acids. As I have already pointed out, it has been suggested that the disease is the result of a deficiency of hydrochloric acid in the gastric juice. While I see no reason to accept this view, I nevertheless think it advisable to satisfy this natural craving when it is present.

The function of the bowels should be carefully regulated. This is a most important point, for although I do not agree with the late Sir Andrew Clark in thinking that the chlorotic condition is the direct result of the constipation with which it is so often associated, there can be no question that careful regulation of the bowels tends to promote recovery. The object of the physician should be to see that the bowels are not only evacuated daily, but that the evacuation is sufficiently copious. Aloin or cascara may be given each night, or some mineral water first thing in the morning, in sufficient quantity to produce a copious and soft but not liquid motion.

When dyspeptic symptoms are prominent, it is of great importance to restore the stomach and gastro-intestinal tract to a normal healthy condition. This is an essential point in the treatment. In the dyspeptic cases, iron is often badly borne or at all events it cannot be given as freely as in others in which there is no dyspepsia. It must, however, be remembered that the dyspepsia which is so frequently associated with chlorosis may be due to different causes. In some cases, the stomach disorder is the result, not the cause, of the anæmia. In such cases, the dyspeptic symptoms disappear with the removal of the chlorosis. As a matter of experience, I find that in those cases of chlorosis in which the tongue is flabby, furred, and indented by the teeth, in which the breath is foul and the patient troubled with flatulence, a preliminary course of alkalies is often most helpful. There is nothing more

efficacious than a combination of bicarbonate of potash, carbonate of soda aromatic spirits of ammonia, tincture of rhubarb and infusion of calumba[1] With this alkaline mixture given before meals, a tonic containing hydrochloric acid, nux vomica, and gentian may be given after meals

As soon as the tongue begins to clean, iron should be freely given In many cases I find that the iron may be given along with these other remedies In some cases I give a bitter tonic before meals and the iron after meals This is, I think, the most effective plan of treatment in those cases in which the dyspeptic symptoms seem to be entirely the result of the chlorotic condition Dr Lauder Brunton has pointed out that in cases of dyspeptic chlorosis the astringent preparations of iron are often better borne than the ordinary forms, but, speaking for myself I find that Robertson's Blaud's pill capsules are in cases of this kind usually well borne I have found this preparation far more efficacious than any other which I have hitherto employed

In those cases in which the stomach is ulcerated, the diet must of course be carefully regulated It should consist of milk beef extracts milk foods and when the symptoms are severe peptonised milk alone Raw beef juice or finely pounded raw meat is in some of the cases well borne A blister should be applied over the region of the stomach the bowels should be carefully regulated in the manner that I have already described and iron and arsenic should be given internally But I need not go into details

In cases of chlorosis the essential part of the treatment is, as I have already mentioned the administration of iron and one great secret of success is to give sufficient iron It matters perhaps comparatively little what the particular preparation is provided only that enough of it is given but some preparations are better borne and more effective than others Personally I have been most successful with Robertson's Blaud's pill capsules These capsules are made of different strengths, corresponding to one two and three Blaud's pills Unless there is any reason to the contrary I begin with the No 2 capsule which contains the same amount of carbonate of iron as three Blaud pills and I give one three times daily after meals, but I do not stop there, I gradually increase the dose During the first week I give one (No 2) capsule three times daily, during the second week two (No 2) capsules during the third week three (No 2) capsules, and during the fourth and succeeding weeks, four (No 2) capsules three times daily,—equivalent to thirty six Blaud's pills per diem In many cases I have given much larger doses even than this In one case which was recently under treatment in hospital, I gave ten No 2 capsules three times daily—equivalent to ninety Blaud's pills per diem. This enormous dose is in the great majority of cases altogether unnecessary, four (No 3) capsules, corresponding to twelve ordinary Blaud's pills, three times daily, are usually quite sufficient

In addition to the iron, I often prescribe arsenic, but I do not attach any great importance to the influence of the arsenic in chlorosis, in this disease iron is a far more efficacious remedy I usually give two minims of Fowler's solution three times a day for the first week, three minims the second, four minims the third, and five minims three times daily during the fourth and succeeding weeks

If the plan of treatment which I have now described is faithfully and diligently carried out, there is in my experience rarely if ever any difficulty in curing even the most severe and obstinate cases of chlorosis, provided of course that no grave or serious complications are present I have I think obtained greater credit and reputation from the treatment of severe and obstinate cases of chlorosis, both in private and hospital practice, than for the treatment of any other disease. I rarely fail to cure even the most severe cases in the course of two or three months

The iron should be continued in full doses until the hæmoglobin as estimated by the hæmoglobinometer, reaches the normal amount—85% to 90% by Gowers' instrument This I consider a most important point No case of chlorosis is really cured until the hæmoglobin has reached the normal, and after this point has been attained, the iron should still be administered for several months in smaller doses—one No. 3 capsule, equal to three Blaud's pills, three times a day.

There are of course, many other preparations of iron which are very effective Griffith's mixture, the saccharine carbonate, the sulphate, the bi-palatinoids of Oppenheimer are all admirable remedies, but with none of them have I obtained such satisfactory results as with Robertson's capsules

In children, in whom a profound anæmia exactly corresponding to the chlorosis of young women is occasionally met with, the saccharine carbonate is perhaps the most effective remedy, it is easily taken and should be freely given A very convenient way is to give it mixed with Demerara sugar.

In dyspeptic chlorosis, I have found a combination of the tincture of the perchloride of iron with sulphate of magnesia a very efficacious form

In the treatment of chlorosis, sulphur is often a valuable remedy, and in the chlorotic condition of young males, which in my experience is often attended with emaciation and dyspeptic symptoms but without much anæmia, this combination of perchloride of iron and sulphate of magnesia is, I think, particularly efficacious In passing, I may also say that it is a most useful remedy in cases in which sores which are difficult to heal break out about the nose, and in cases of recurring boils In many of these conditions, the symptoms are probably due to absorption into the blood of poisonous products developed in the intestine In cases of this kind, constipation is often a prominent symptom. The combination of perchloride of iron and sulphate of magnesia acts both as a laxative, an intestinal disinfectant, and as a blood tonic.

Other remedies which have been recommended for the treatment of chlorosis are oxygen inhalations and the administration of bone marrow. I have no personal experience to offer with regard to either of them. I am so successful with the rest-iron plan of treatment, which I have described above, that I have

[1] This alkaline mixture which I give largely and with great advantage in cases of chronic gastritis and flatulent dyspepsia is as follows —

℞.—Potassii Bicarb
Sodæ Carb
Sp Ammon Arom ā ℥ss
Tr Rhei ℥ij
Inf Calumbæ ad ℥vi
Sig.—A tablespoonful in water three times daily twenty minutes before meals

* Messrs Robertson inform me that they attribute the medicinal value of the preparation to the use of the dried salts and the medium used for forming the mass The disintegration being gradual, the nascent ferrous carbonate is slowly formed in the stomach and is as quickly absorbed by the system, and hence the good results. That the ferrous carbonate is formed after the administration is, they say, also proved by the slight aperient effect which the capsules have, owing to the formation of an alkaline sulphate They claim that this aperient action does away with the necessity of patients having to take an aperient; but with this opinion my experience does not altogether agree.

never found it necessary to give any other plan of treatment a prolonged trial

In the course of three or four weeks, the patient may be allowed to get out of bed and to pass part of the day on a sofa or to take carriage exercise In cases of chlorosis walking exercise is, I think, better avoided, so long, at all events, as the heart symptoms—the shortness of breath on exertion, the palpitation, etc—continue. As the colour returns and the hæmoglobin increases, the patient may gradually be allowed to return to her ordinary mode of life

During the earlier part of the treatment while the patient is confined to bed, massage is often a valuable adjunct to the treatment It promotes the muscular nutrition and gives the patient, as it were, a sufficient amount of exercise without throwing any strain upon the heart

It is essential to remember that chlorosis is a condition which is very apt to relapse. As I have already stated, the iron should be continued for some time—several months at least—after the hæmoglobin has reached the normal percentage, and after all treatment has been suspended the patient should be closely watched for a year or two at least If any indications of a relapse (such as breathlessness, palpitation, pallor, etc), again develop, another course of iron should be immediately prescribed, but, provided that the onset of the relapse is recognised at an early stage, it is rarely necessary to confine the patient to bed Careful regulation of the bowels, avoidance of cardiac strain and the administration of iron are, in such circumstances, usually all that are required to effect a cure

I have described the treatment of chlorosis in considerable detail, it is an important subject, for the disease is very common and it is a most satisfactory disease to treat Niemeyer used to say that he gained great credit in practice by the successful administration of Blaud's pills, and, as I have already stated, my personal experience is identical with his on this point

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THE CLINICAL INVESTIGATION OF CASES OF CHLOROSIS

In studying cases of chlorosis during life, the following points in particular should be noticed —

Preliminary Facts —Name Age Sex Married or single (if married, number of children or miscarriages) Occupation Station in life Circumstances and surroundings (whether well fed, well clothed, well housed, accustomed to heavy work, exposed to mental strain, etc) Place of residence Place of birth Date of examination Complaints

Family History —Whether any of the patient's near relatives have suffered from chlorosis or any other form of profound anæmia Whether the patient inherits a tendency to any special form of disease (phthisis, etc)

Personal History and Etiology —The condition of the patient's health prior to the date at which the first symptoms of the disease (chlorosis) were developed The nature and date of any previous illnesses The date at which menstruation was established Whether the mammæ and genital organs were developed when menstruation was established Whether the disease was slowly and gradually or rapidly developed Whether there was any apparent cause for the development of the disease, such as dyspeptic troubles, constipation, uterine derangement, mental anxiety, strain, tight lacing, etc

The mode of onset and order of development of the symptoms —The exact date at which the first symptoms were noticed The nature of the first symptoms (pallor, shortness of breath, palpitation, etc).

Present Condition and Symptomatology

1 *The symptoms of which the patient complains* —(Debility, shortness of breath on exertion, palpitation, giddiness, tinnitus aurium, pain in the stomach, dyspepsia, constipation, amenorrhœa, swelling of the feet, etc)

2. *Colour of the skin and mucous membranes.*—(Pallor, greenish tint, etc).

3 The *complexion* (dark, fair, etc).

4 *The general state of nutrition* (well or ill nourished, whether the body fat is preserved, whether the muscles are soft and wasted, the condition of the nails, hair, etc.).

5 *The temperature.*

6. *The condition of the blood* —(a) Appearance of a drop of blood obtained by puncturing the unbandaged finger (b) The number of the red blood corpuscles (c) The total percentage of hæmoglobin (d) The individual richness of the red blood corpuscles in hæmoglobin (e) The number of the white corpuscles (f) The microscopical character of —the red blood corpuscles—whether they form rouleaux, their colour, size—(megalocytes, microcytes) their shape—(poikilocytosis), concentration of hæmoglobin in localised areas of, vacuolation of, nucleated red corpuscles, deeply stained red corpuscles of small size (Eichhorst's corpuscles) The white corpuscles (size, shape, etc) Max Schultze's granular masses. Blood platelettes, etc

7 *Hæmorrhages* —The presence of retinal hæmorrhages, hæmatemesis, etc

In examining the retina with the ophthalmoscope, the condition of the optic discs (colour, presence of swelling, papillitis, etc), should be noted

8 *The condition of the circulatory organs* —Whether the action of the heart is unduly irritable, the position of the apex beat, the nature of the cardiac impulse (diffused, flickering, etc), the size of the heart is determined by percussion, the presence or absence of cardiac murmurs in the mitral, pulmonary, tricuspid and aortic areas, their rhythm, sound, characters, etc

The exact condition of the pulse (frequency, fulness, regularity, etc)

The presence of a venous hum in the neck, etc , the presence of distended veins or of true pulsation in the veins of the neck, etc

9 *The condition of the digestive system* —Anorexia, thirst, pain after food, nausea, vomiting, hæmatemesis, pain and tenderness in the epigastrium, constipation, etc The condition of the tongue (clean, furred, pale, indented by the teeth, etc) The presence or absence of piles The condition of the liver and spleen

10 *The condition of the urine*

11 *The condition of the nervous system* —Giddiness on effort, irritability of temper, hysterical symptoms, etc

12 *The condition of the respiratory system*

13 *The condition of the generative organs.*—Menstruation (date at which it was established, regularity, amount of discharge, colour of discharge, etc)

Treatment —The treatment adopted and its results

The subsequent progress of the case —The red blood corpuscles should be counted, the hæmoglobin estimated and the microscopical characters of the blood noted at least once every week

Intercurrent complications

Total duration

Result —The condition of the blood at the end of the treatment should be particularly noted.

PERNICIOUS ANÆMIA

Synonyms.—Idiopathic anæmia; Essential anæmia; Progressive pernicious anæmia; etc.

THIS very interesting disease is characterised by profound anæmia, which usually develops insidiously and without apparent cause. It tends to pursue a progressive course and with rare exceptions ultimately terminates in death. The celebrated Dr. Addison of Guy's Hospital, the discoverer of Addison's disease, was the first to give a complete description of it; he termed it *idiopathic anæmia*.

Though well known to Dr. Wilks and other English physicians, it was for a time lost sight of until it was redescribed by Biermer in the year 1872. Of recent years numerous cases have been recorded, and our knowledge of the disease has been very materially increased. In 1876, I published a series of cases in the *Edinburgh Medical Journal*. In that paper I figured the blood changes and directed attention to the value of arsenic in the treatment of the disease.

The essential feature of pernicious anæmia is the great diminution in the number of the red blood corpuscles. The total amount of hæmoglobin in the blood is also markedly decreased, but the diminution of the hæmoglobin is less than that of the corpuscles; in fact, the richness of the individual corpuscles in hæmoglobin is in most cases above the normal.

In many typical cases of pernicious anæmia the essential and primary change seems to be a destruction of the red blood corpuscles in the portal system of vessels. Dr. William Hunter, whose observations have added so much to our knowledge of the pathology of the disease, thinks that the blood destruction is due to the absorption of a poison from the gastro-intestinal tract; and that this poison leads to the rapid destruction of the red blood corpuscles in the portal circulation (the spleen and liver) and at the same time exerts a disturbing influence upon the liver cells. Some years ago, I ventured to suggest to Dr. Hunter that if his view was correct the disease might be appropriately termed *gastro-intestinal-hepatic* anæmia.

Before considering the pathology of pernicious anæmia in detail, it will perhaps be advisable to describe the clinical features of the disease and the morbid alterations which are present in the bodies of patients who have died of the disease.

The Clinical Features of Pernicious Anæmia.—Addison's description of pernicious anæmia, or idiopathic anæmia as he termed it, was as follows:—

'As a preface to my subject, it may not be altogether without interest or unprofitable to give a brief narrative of the circumstances and observations by which I have been led to my present convictions.

'For a long period I had from time to time met with a very remarkable form of general anæmia occurring without any discoverable cause whatever, cases in which there had been no previous loss of blood, no exhausting diarrhœa, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, strumous, or malignant disease.

'Accordingly, in speaking of this form in clinical lectures, I, perhaps with little propriety, applied to it the term "idiopathic" to distinguish it from cases in which there existed more or less evidence of some of the usual causes or concomitants of the anæmic state.

'The disease presented in every instance the same general character, pursued a similar course, and, with scarcely a single exception, was followed after a variable period by the same result.

'It occurs in both sexes; generally, but not exclusively, beyond the middle period of life; and, so far as I at present know, chiefly in persons of a somewhat large and bulky frame, and with a strongly-marked tendency to the formation of fat.

'It makes its approach in so slow and insidious a manner that the patient can hardly fix a date to his earliest feeling of that languor which is shortly to become so extreme. The countenance gets pale, the whites of the eyes become pearly, the general frame flabby rather than wasted; the pulse perhaps large, but remarkably soft and compressible, and occasionally with a slight jerk, especially under the slightest excitement. There is an increasing indisposition to exertion, with an uncomfortable feeling of faintness or breathlessness on attempting it; the heart is readily made to palpitate; the whole surface of the body presents a blanched, smooth, and waxy appearance; the lips, gums, and tongue seem bloodless; the flabbiness of the solids increases; the appetite fails; extreme languor and faintness supervene, breathlessness and palpitations being produced by the most trifling exertion or emotion; some slight œdema is probably perceived about the ankles. The debility becomes extreme; the patient can no longer rise from his bed; the mind occasionally wanders; he falls into a prostrate and half-torpid state, and at length expires. Nevertheless, to the very last, and after a sickness of perhaps several months' duration, the bulkiness of the general frame and the obesity often present a most striking contrast to the failure and exhaustion observable in every other respect.

'With perhaps a single exception, the disease, in my own experience, resisted all remedial efforts, and sooner or later terminated fatally.

'On examining the bodies of such patients after death I have failed to discover any organic lesion that could properly or reasonably be assigned as an adequate cause of such serious consequences; nevertheless, from the disease having uniformly occurred in fat people, I was naturally led to entertain a suspicion that some form of fatty degeneration might have a share at least in its production; and I may observe that, in the case last examined, the heart had undergone such a change, and that a portion of the semilunar ganglion and solar plexus, on being subjected to microscopic examination, was pronounced by Mr. Quekett to have passed into a corresponding condition.

'Whether any or all of these morbid changes are essentially concerned—as I believe they are—in giving rise to this very remarkable disease, future observation will probably decide.

'The cases having occurred prior to the publication of Dr. Bennett's interesting essay on "Leucocythæmia," it was not determined by microscopic examination whether there did or did not exist an excess of white corpuscles in the blood of such patients.

'It was whilst seeking to throw some additional light upon

this form of anæmia that I stumbled upon the curious facts which it is my more immediate object to make known to the profession." [1]

From this account, it will be seen that the onset is, as a rule, gradual and the course progressive; that in many cases the condition arises without any apparent cause; that it is chiefly characterised by increasing pallor, a profoundly bloodless condition of the mucous membranes and other tissues and organs, debility, shortness of breath, palpitation, œdema of the feet, and, I may add, retinal hæmorrhages, recurring attacks of fever, etc. In the advanced stages of the disease, there may be some swelling of the face, hands, and subcutaneous tissues generally, but a marked degree of general dropsy is rarely present.

Let us take a typical case in a fully developed stage and consider some of the symptoms in more detail.

Colour of the skin and mucous membranes.—In well-marked cases of pernicious anæmia, the observer is at once struck by the remarkable pallor of the mucous membranes and of the skin. The skin rarely presents the white pallor which is seen after hæmorrhage or in cases of Bright's disease; it usually has a lemon-yellow tint. In some cases this yellow tint is so marked that the patient looks as if he were jaundiced. As a matter of fact, jaundice does occasionally occur, but in the great majority of cases the yellow colour of the skin is not due to jaundice. This is a point of some importance from an etiological point of view, as we shall presently see. In the great majority of cases, the conjunctiva is not stained with bile pigment, although it is quite common to find the conjunctiva yellow in localised spots, usually about the inner canthus. The yellowness of the conjunctiva is usually due, as I pointed out several years ago, to deposits of subcutaneous fat. In those cases in which true jaundice occurs, the whole of the conjunctiva is of course stained yellow. I recently had under observation an interesting case of this kind.

The general state of nutrition.—In most cases of pernicious anæmia emaciation is not a prominent symptom, though exceptions to this general statement are occasionally met with. The subcutaneous fat is usually well preserved; the muscles are soft and flabby and more or less (in some cases considerably) wasted, but the marked emaciation which is so characteristic of malignant disease is rarely present. This is a point of considerable diagnostic importance, for in some cases it is by no means an easy matter to distinguish pernicious anæmia and cancer of the stomach. The skin has usually a soft velvety feel—another point of distinction between pernicious anæmia and cancer of the stomach, for in malignant disease the skin is usually wrinkled and atrophied and often dry and harsh.

Hæmorrhages.—In advanced cases of pernicious anæmia, hæmorrhages are of frequent occurrence. Epistaxis, bleeding from the throat and gums are the most frequent. Bleeding from the uterus and vagina is not uncommon. In rare cases, there is hæmorrhage from the bowel or stomach. In the advanced stages of the disease, petechial hæmorrhages are sometimes found in the skin; and in most well-marked cases of the disease, hæmorrhages are present in the retina. (See Plate XCIV. Figs. 2 and 3.) The presence of retinal hæmorrhages is of considerable diagnostic importance. In exceptional cases there is some swelling and inflammation of the optic discs (papillitis).[1] As I shall presently point out, hæmorrhages beneath the pericardium, the pleura, and into the delicate tissue of the brain are very generally present in the bodies of patients who have died from the disease.

Febrile attacks.—During the course of pernicious anæmia temporary attacks of pyrexia are of frequent occurrence and of considerable diagnostic value. In some cases, the fever is continuous; in others, intermittent or remittent. The fever has been termed anæmic fever or the essential fever of anæmia. In many cases it seems to be associated with a rapid destruction of red blood corpuscles, which is apt to occur from time to time in what may be termed a paroxysmal manner. During these paroxysms there is usually an exacerbation of the symptoms and the urine often becomes deeply pigmented.

The condition of the urine.—In most cases of pernicious anæmia which have come under my own notice the urine has presented no abnormal appearance; it has been as a rule normal in colour or paler than normal; during the paroxysmal exacerbations and in the advanced stages of the disease it may, as I have already mentioned, be more deeply coloured than normal. In some cases at all events this excessive pigmentation appears to be due to the presence of pathological urobilin. Dr. William Hunter and Dr. Mott think that the deep pigmentation of the urine is an important clinical indication of the excessive blood destruction which is taking place. When the blood destruction is excessive, part of the pigment is excreted by the kidneys; and after death microscopical deposits of iron have been found in the renal tubules. Dr. Hunter states that in some cases in which the urine is highly coloured not only is pathological urobilin present in the urine in large quantities, but the presence of blood pigment may be recognised in the urine in the form of microscopical granules and on analysis the iron excreted in the urine is increased in amount.

In some cases, the uric acid is in great excess; a very marked case of this kind came under my observation a few years ago.

The condition of the heart and pulse.—In well-marked cases of pernicious anæmia, the cardiac cavities are dilated and the heart muscle is found after death to be in an advanced state of fatty degeneration; there is, in fact, no disease in which fatty degeneration of the heart is so marked as in pernicious anæmia. As in chlorosis, the heart muscle is abnormally irritable and weak.

The pulse frequency is usually increased; the pulse is soft, of low tension and often dicrotic in character; in the advanced stages of the disease the pulse may present a jerking character which to an inexperienced observer may suggest the presence of aortic regurgitation. Trivial excitements are apt to increase the frequency of the pulse and to produce palpitation.

A venous hum is present in the neck. In the advanced stages of the disease the external jugular veins are often knotted and distended, or the seat of true venous pulsation indicative of tricuspid regurgitation.

A systolic murmur is present in the pulmonary area; in

[1] The passage is taken from Addison's remarkable treatise 'On the Constitutional and Local Effects of Disease of the Suprarenal Capsules.' It was while trying to discover the cause of this idiopathic anæmia, as he termed it, that he came to discover and describe the disease of the suprarenal capsules which bears his name.

[1] In cases of anæmia, the occurrence of hæmorrhages seems to depend chiefly upon the number of red blood corpuscles which are present. Whenever the red blood corpuscles remain for any time below 50%, hæmorrhages are apt to occur. In profound cases of pernicious anæmia—a chronic form of anæmia—in which the red blood corpuscles are reduced to one million per cubic millimetre or even less, the occurrence of hæmorrhages into the retina has in my experience been almost invariable; in such cases, hæmorrhages into the other tissues of the body and bleeding from external surfaces are also common.

many cases a systolic murmur may also be heard in the mitral tricuspid and, less frequently, in the aortic areas. The cardiac impulse is diffused, feeble, flickering, and the transverse dulness in particular increased. In many cases the lungs are emphysematous and the increased area of cardiac dulness is less marked than one would expect from the appearance of the heart after death. The condition of the heart is, in short, identical with that which is met with in chlorosis; but in the advanced stages of pernicious anæmia the cardiac alterations are even more marked and the heart symptoms more prominent than in aggravated cases of chlorosis.

The condition of the digestive system.—Symptoms indicative of functional derangement of the stomach and intestines are almost invariably present. Anorexia is usually a prominent symptom. Nausea and vomiting, which often occur in paroxysms, are common symptoms. In some cases there is constipation; in others there is diarrhœa. In several cases of pernicious anæmia which have come under my own notice, the development of the disease has been preceded by intractable diarrhœa; and in more than one of these cases I have found the intestines ulcerated after death. I am disposed to think that prolonged diarrhœa is in some cases an important factor in the production of the disease.

The tongue is usually very pale; in many cases, it is unusually smooth, apparently destitute of its surface epithelium, but not raw-looking; in other cases, it is flabby and indented by the teeth; in some cases it is furred; in the later stages of the disease it is frequently dry. During the later stages of the disease the patient often suffers from distressing thirst.

The condition of the nervous system.—Giddiness on rising from the recumbent to the erect position and on stooping, fainting on slight exertion, or after a free evacuation of the bowels, etc., are very common symptoms. The temper is in many cases unduly irritable. The patient is unable to carry on any sustained mental effort; he easily becomes exhausted and tired. The memory is in some cases impaired. Tinnitus aurium, throbbing in the head and headache are common symptoms. In the advanced stages of the disease, an extremely distressing and painful condition of uneasiness and restlessness is often present. Finally, the patient may pass into a drowsy semi-comatose condition; in other cases, epileptiform convulsions or profound coma occur. It is needless to say that these symptoms are usually the precursors of death.

The condition of the blood.—This is most important. Owing to the profoundly bloodless condition, it is often impossible by simply puncturing the finger, to obtain a sufficient amount of blood for the purpose of accurate examination. A prick may produce little or no bleeding. When a drop of blood is obtained by a simple puncture in this way, it is usually seen to be thin and watery-looking; it looks like very thin claret, and often immediately separates into a clear watery part and a more deeply stained part, the colour of which is, however, almost invariably markedly below that of normal blood. In order to obtain a drop of blood of sufficient size for the purposes of accurate examination, it is usually necessary, after making the patient hang the hand down over the side of the bed, so as to allow the blood to gravitate into the tips of the fingers, to bandage one of the fingers tightly from the meta-carpo-phalangeal joint down to the termination with a strip of tape. In this way all the blood which is contained in the finger is collected in the tip. Owing to the concentration of the corpuscles, the drop of blood which is now obtained by a deep puncture in some cases appears to be much more normally coloured, and the number of corpuscles is much larger than in a drop of blood obtained by simple puncture, i.e. without bandaging the finger.

On examining the blood, characteristic changes are found. The most striking alteration is the diminution in the number of red blood corpuscles. In well-marked cases of pernicious anæmia the red blood corpuscles, instead of numbering 5,000,000 or 5,500,000 per cubic millimetre, are usually found to be reduced to less than 1,500,000. It is quite common to find only 1,000,000 or less. In many cases only 500,000 red corpuscles are present, and in one case described by Quincke, the number of red blood corpuscles only reached 143,000; but as Dr. Stephen Mackenzie has pointed out, Quincke's figures always read low. In the great majority of cases in which the red blood corpuscles have been reduced to 500,000 per cubic millimetre, the patient has died from the disease. In Quincke's case recovery took place.

The total amount of hæmoglobin is always markedly reduced in the advanced stages of the disease, but the reduction of the hæmoglobin is relatively less than that of the red blood corpuscles. The individual richness of the red blood corpuscles is consequently usually above the normal. In a case, for example, which I had under observation when this paper was written, the red blood corpuscles numbered 1,125,000 per cubic millimetre, while the hæmoglobin estimated by Gowers' instrument equalled 31%. This gives the following fraction:— $\frac{H}{R.C.}=\frac{31}{25}$, instead of $\frac{H}{R.C.}=\frac{90}{100}$.[1] These characteristics are of the greatest diagnostic importance; they are the direct opposite of the condition of the blood in chlorosis. I will return to this point when I come to speak of the diagnosis.

The microscopical alterations which the red blood corpuscles present are also of great diagnostic significance. There is no disease in which the red blood corpuscles are so markedly altered in size and shape as in pernicious anæmia. The red blood corpuscles do not go into rouleaux; some of them are larger than normal—megalocytes; others are smaller than normal—microcytes. Many of them are tailed, pear-shaped, battledore-shaped, biscuit-shaped, etc. (See Plate XCIV. Fig. 1.)

In some cases, nucleated red blood corpuscles are present. In the original series of cases of pernicious anæmia which came under my observation in the year 1876, I published a plate illustrative of these changes in the blood. So far as I know, this was the first time that these changes, which had been previously described by other observers, had been actually figured. In that drawing, I represented many of the blood corpuscles as nucleated. I now know that the nucleated appearance was, for the most part, apparent only. The appearances which I supposed were indicative of a nucleus were soon afterwards shown by Drs. Mackern and Davy to be due to a concentration of the hæmoglobin in a particular part of the corpuscle. It is certain, however, that in many cases of pernicious anæmia, nucleated red blood corpuscles are actually present. Some of the red blood corpuscles appear to contain

[1] As I have already pointed out, the hæmoglobin as estimated by Gowers' instrument rarely if ever, even in health, equals 100 per cent. It usually only equals (in my experience) 85-87 per cent. in health. To allow for fallacies I have put it in the fraction given above (as representing normal blood) at 90 per cent. It is obvious that in the fraction $\frac{31}{25}$ the corpuscular richness in hæmoglobin is under-estimated. It ought to be 34·4% instead of 31%.

vacuoles. Deeply stained microcytes, which were first described by Eichhorst and which when present are of considerable diagnostic importance, are in some cases present; but in my experience they are much more rare than some observers indicate.

It is said that in some cases of pernicious anæmia, organisms have been present in the blood; in more than one case of the disease, flagellated organisms have been described. In some cases which have come under my own notice, I have seen appearances which seemed to me suggestive of organisms, but up to the present time I have not been able in any single case to make sure of their presence.[1] The blood platelettes are often more numerous than normal.

Max-Schultze's granular masses are usually present, and the white blood corpuscles are, as a rule, normal, though in some cases they are slightly increased, more particularly towards the termination of the disease.

In some of the cases which I have observed, the white blood corpuscles have usually been smaller than normal. They seemed to be chiefly composed of lymph corpuscles.

The hæmoglobin stability is remarkably impaired. I have already pointed out that the hæmoglobin tends to become concentrated in a particular part of the corpuscle and to give an appearance of apparent nucleation. Dr. Copeman has also shown that the hæmoglobin tends to separate readily out of the corpuscles when the blood is removed from the body; this appears to be an important point in connection with the pathology of the disease.

Such, then, are the most important microscopic changes in the blood. Though highly significant and characteristic of the disease, it is important to remember that these changes are not pathognomonic; they may occur in any condition in which the red blood corpuscles are profoundly reduced in number, and in which the red-blood-forming organs are called upon to rapidly produce an excessive number of red blood cells. As a result of the excessive strain the production is imperfect and many immature and imperfectly-formed red blood corpuscles are thrown into the circulation.

Etiology.—Pernicious anæmia usually occurs in adults, most frequently, so far as my experience enables me to judge, between the ages of 45 and 60; it is very rare before the age of 20 and in advanced old age. Both sexes are perhaps equally liable to be affected; in some of the tabulated lists of cases which have been published, females were more frequently affected than males; but in the majority of cases which have come under my own observation the patients were males. The disease seems to occur in all countries and in persons of all occupations. The great majority of cases which have come under my own notice of recent years have occurred in well-to-do people, but it is probable I think that the disease is more common amongst the lower orders of society and those whose social habits and surroundings are unsatisfactory.

In many of the reported cases the patients have, up to the onset of the disease, enjoyed good health. In a considerable number of cases, the disease is preceded by dyspeptic troubles and diarrhœa. In many cases the onset has been preceded by mental anxiety, strain, etc. In some cases the patients have suffered from a prolonged drain of blood. A profound form of anæmia, somewhat similar to that characteristic of pernicious anæmia appears sometimes to be developed as the result of long-continued malarial poisoning. Two of my patients had previously suffered from yellow fever. A profound condition of anæmia, resembling pernicious anæmia, may also be developed after prolonged lactation, pregnancy and parturition. In some cases, intestinal parasites (the ankylostomum duodenale and the bothriocephalus latus) have been found in the intestine. A profound form of anæmia, which in many of its clinical features closely resembles pernicious anæmia, was very prevalent amongst the miners in the St. Gothard tunnel, and was proved to be due to the ankylostomum duodenale; in these cases the anæmia seems to be the direct result of the abstraction of blood from the intestinal mucous membrane. In some cases the condition appears to be developed in patients affected with cancer of the stomach, but this is rare.

Morbid Anatomy.—Before considering the exact manner in which the anæmia is produced, it may perhaps be well to direct attention to the morbid anatomy of the disease.

The bodies of patients who have died of pernicious anæmia are remarkably bloodless; the brain is more anæmic than in any other condition, death from hæmorrhage not excepted. In more than one case I have diagnosed pernicious anæmia in the post-mortem room from the bloodless condition of the brain alone.[1] The heart and large vessels usually contain little or no blood. The heart muscle is in a condition of advanced fatty degeneration. The somatic muscles are in some cases of a deep red colour, like the muscles of a horse. The bone marrow is often altered in a way which I will presently describe. Petechial extravasations are usually present in the pericardium, pleura, on the surface of the brain and in the retina.

These are the chief naked-eye alterations.

In a considerable proportion of cases morbid changes are present in the stomach or intestine. The mucous membrane of the stomach is sometimes atrophied; in others affected with fibroid change. In two of my cases it presented a mammillated appearance towards the pylorus. Ulceration of the intestine is sometimes present. Worms or other parasites are sometimes found in the intestine.

The spleen is in most cases somewhat enlarged; in a few shrunken. Dr. Hunter has suggested that the difference depends upon the condition as regards blood destruction which was going on just before death.

The liver is fatty and on microscopical examination presents in most typical cases a highly important and characteristic alteration, viz. the presence of pigment granules, which consist of iron, in the outer two-thirds of the portal area. According to Dr. William Hunter, this change is characteristic and pathognomonic of pernicious anæmia. In two of the cases which I described many years ago, I recognised the abnormal pigmentation but I did not attach any importance to it.

Whether this excess of iron in the liver is, as Dr. Hunter supposes, a constant feature of pernicious anæmia remains to

[1] In one case, observed some years ago, a series of cultivations were made. A very definite growth was obtained in gelatine tubes. Dr. Hare of Manchester kindly examined the specimens for me and stated that they consisted of a short thick bacillus with rounded ends which was growing very rapidly. He further stated:—'I cannot recognise it (the bacillus) as any with which I am acquainted, but from its character and rapidity of growth I am inclined to think it saprophytic.'

[1] Without of course knowing anything of the clinical history or seeing the whole of the post mortem—going into the pathological theatre, seeing the exposed brain—I have, from the remarkably bloodless condition, said to the pathologist, 'That is surely a case of pernicious anæmia.'

be proved by further observation. In one case which presented all the typical clinical characters of pernicious anæmia, Dr. W. B. Ransom found no excess of iron in the liver after death. I have no post-mortem observations of my own to offer on the point, for it is a remarkable fact that since Dr. Hunter's observations were published I have had the opportunity of examining only one case of pernicious anæmia after death. Portions of the liver and other tissues from that case were sent to Dr. Hunter who kindly examined them and found that they were typical and characteristic. As I shall presently point out, I am disposed to think that the clinical condition, pernicious anæmia (or as Dr. Hunter would probably say, a profound anæmia undistinguishable during life from pernicious anæmia) may be due to other conditions than excessive blood destruction in the portal area; and if this is so it must of course be admitted that an excess of iron in the liver is not an essential feature of the disease.

The marrow of the bones is in many cases diseased; the yellow marrow is replaced by red marrow, and the marrow tissue is evidently in a state of active change and proliferation.

Pathological changes are sometimes present in the spinal cord. In some cases, they consist of patches of myelitis, in all probability produced around minute petechial hæmorrhages. In other cases, the posterior columns are sclerosed very much in the same way as they are in locomotor ataxia. In others, again, the crossed or direct pyramidal tracts are sclerosed. In most cases in which the degeneration is advanced there is, as Dr. James Taylor has shown, a condition of postero-lateral sclerosis, very similar in appearance and distribution to the lesions in cases of ataxic paraplegia. It remains, however, to be shown whether in cases such as he has described (in which the pathological changes in the spinal cord were very marked and striking) the anæmia was the cause of the cord changes; and, if so, whether the anæmia was 'pernicious.' Dr. Taylor thinks that these extensive cord lesions are probably the result of some toxic substance. This view seems to me very probable.

Pathological Physiology.—There is still considerable difference of opinion as to the exact manner in which the anæmia is produced—in other words, as to the exact nature and causation of the condition which is termed pernicious anæmia. In the present state of our knowledge it is perhaps impossible to come to a positive conclusion and to give an explanation which will embrace all cases. In considering the nature and causation of the disease, the following questions have to be taken into account:—

1. Is the condition which we term pernicious anæmia a separate and distinct disease, or may the *clinical* condition which we term pernicious anæmia be the result of several different pathological conditions and morbid states?

2. Is the anæmic condition the result of blood destruction or defective blood formation?

3. What is the fundamental and underlying cause of the condition?

All of these questions are more or less intimately bound up together, and it is difficult to answer one without considering and answering the others. In the present state of our knowledge it is perhaps impossible to give a decided and dogmatic answer to any one of them.

Dr. William Hunter is of opinion that there is a separate and distinct disease, pernicious anæmia; that it is due to blood destruction; that the blood destruction takes place in the portal circulation; that it is no mere exaggeration of that which occurs in health, but that its characters can only be reproduced experimentally by special poisons; and that the blood destruction is the result of the absorption of some poisonous substance, probably a chemical substance or cadaveric ptomaine, produced in the intestine by micro-organisms. He considers it as 'a specific form of gastro-intestinal infection.' He thinks that within the portal area the chief blood destruction occurs in the spleen and liver; and that the hæmoglobin which is liberated from the red corpuscles, thus destroyed, is carried to the liver and is for the most part stored up in abnormal quantity in the form of blood pigment in the liver cells in the outer two-thirds or portal zone of the lobule, instead of being mainly, as it is in health, converted by the liver cells into bile pigments and urinary pigments. In certain cases, however, part of it escapes through the liver into the general circulation and is broken up into blood pigment within the epithelium of the convoluted tubules in the course of its excretion through the kidney.

Dr. Hunter summarises his conclusions in the following propositions:—

'1. Pernicious anæmia is to be regarded as a special disease both clinically and pathologically. It constitutes a distinct variety of *idiopathic* anæmia.

'2. Its essential pathological feature is an excessive destruction of blood.

'3. The most constant anatomical change to be found is the presence of a large excess of iron in the liver.

'4. This condition of the liver serves at once to distinguish pernicious anæmia post mortem from all varieties of *symptomatic* anæmia, as also from the anæmia resulting from loss of blood.

'5. The blood destruction characteristic of this form of anæmia differs both in its nature and its seats from that found in malaria, in paroxysmal hæmoglobinuria, and other forms of hæmoglobinuria.

'6. The view can no longer be held that the occurrence of *hæmoglobinuria* simply depends on the quantity of hæmoglobin set free.

'7. On the contrary, the *seat* of the destruction and *the form assumed by the hæmoglobin* on being set free are important conditions regulating the presence or absence of hæmoglobinuria in any case in which an excessive disintegration of corpuscles has occurred.

'8. In paroxysmal hæmoglobinuria the disintegration of corpuscles occurs in the general circulation, and is due to a rapid dissolution of the red corpuscles.

9. In pernicious anæmia the seat of disintegration is chiefly the portal circulation, more especially that portion of it contained within the spleen and the liver, and the destruction is effected by the action of certain poisonous agents, probably of a cadaveric nature, absorbed from the intestinal tract.'

Dr. Hunter regards the changes in the bone marrow as secondary to the blood destruction. Before I became acquainted with his observations, I was in the habit (with, I suppose, most other clinicians and pathologists) of regarding the great diminution in the number of the red blood corpuscles, which is the essential characteristic of pernicious anæmia, as the result of defective blood formation. The presence of large numbers of immature red blood corpuscles and the presence in the blood of nucleated red blood corpuscles seemed to me to be strongly in favour of this view—defective formation rather than of increased destruction. At the time when Dr. Hunter first told me of his experiments and observations, I had the advantage of his assistance in the Out-patient Department of the Edinburgh Royal Infirmary. I put the question to him, 'How do you account for the large number of immature red blood corpuscles in the blood?' He met this by saying that if you have excessive destruction of red blood

corpuscles at one end of the circulation (i.e. in the portal circulation), there is all the greater necessity for excessive production at the other (i.e. in the bone marrow); in other words, he explained the defective formation of the red blood globules as the result of the excessive strain thrown on the blood-forming tissues—the bone marrow. This argument, which supposes that a large number of immature and imperfect red blood cells were thrown into the circulation in order to meet, as it were, and compensate the excessive blood destruction which was going on at the other end of the circulation, seemed to me a satisfactory explanation; but the question is whether it represents the whole truth.

It is quite possible, I think, that in many cases of pernicious anæmia the diminution of the red blood corpuscles is the result both of excessive destruction and defective formation. Even if we admit with Dr. Hunter that in the great majority of cases of pernicious anæmia the primary cause of the anæmia is excessive blood destruction, it must, as I have already stated, be allowed that there is imperfect and defective blood formation in the bone marrow. Now, it is not difficult to conceive, if this condition (imperfect and defective formation of red blood corpuscles, due to an excessive and pathological strain, so to speak, on the bone marrow) continues and lasts, as we know it must do, for long periods of time, that an actual diseased condition of the bone marrow may ultimately become produced. We may suppose that there is, in the first instance, as the result of the excessive strain which is thrown upon the bone marrow, a condition of irritable weakness; and that this, as in many other cases of irritable weakness, may ultimately pass on to organic disease. It seems to me probable that although the fundamental change in many cases of pernicious anæmia (those—and they seem to comprise the great majority of cases—in which there is an excess of iron in the liver) is the result of blood destruction in the portal circulation, the defective formation in the bone marrow is an important consideration which cannot be ignored. To cases of this kind in which there is an excess of iron in the liver, the term 'gastro-intestinal-hepatic type of hæmolytic anæmia' may I think be appropriately applied. I think it probable that even in these cases—the Hunterian type of the disease—a double cause for the bloodlessness is present, viz. increased blood destruction in the portal circulation and defective blood formation in the bone marrow.

Further, there seems reason to suppose that in some cases a primary lesion of the marrow of the bone may lead to the production of a form of anæmia which is very closely allied to, if not identical with, the pernicious variety of the disease. If this is so, we may term these cases the myeloid type of pernicious anæmia of hæmogenetic origin. And in this connection it is interesting to note that twenty years ago Professor Pepper of Philadelphia proposed the term 'myelogenous anæmia' for the disease.

But further, if it be admitted, as I have suggested above, that long-continued and excessive blood destruction, however produced, may ultimately lead to an abnormal and diseased condition of the red-blood-forming tissue (the bone marrow), it must be allowed that the clinical group of symptoms to which we give the term pernicious anæmia may be due to a variety of processes.

This view seems to me supported by the fact that a *clinical* condition, undistinguishable from pernicious anæmia, may be developed as the result of a prolonged drain of blood from the body. A well-marked case of this kind came under my observation some years ago. The patient had suffered for years from a bloody vaginal discharge, the result of a diseased condition of the ovary and uterus. She was profoundly anæmic, the red blood corpuscles were of all shapes and sizes, in short the microscopic condition of the blood exactly corresponded to that which is characteristic of pernicious anæmia. In this case the excessive and long-continued loss of red blood corpuscles from the uterus was apparently the cause of an excessive and imperfect formation of red blood corpuscles in the bone marrow, while the resulting anæmia was clinically speaking undistinguishable from the anæmia characteristic of the usual (Hunterian) type of the disease. *Pathologically* it would no doubt have been distinguished by the absence of an excess of iron in the liver or kidney.

I am not then prepared to deny that a drain of blood, which lasts for a sufficiently long period of time, may not ultimately produce a form of anæmia which is clinically identical, so far as the condition of the blood is concerned and so far as our present methods of examination enable us to judge, with pernicious anæmia. But notwithstanding this opinion, I am quite unable to agree with the theory which Dr. Stockman has advanced that pernicious anæmia is due to the small capillary hæmorrhages which are such a striking pathological feature in most fatal cases of the disease. I look upon these capillary hæmorrhages as a consequence—the result—not the cause of the anæmia.

Now, in such a case as that described above, in which a form of anæmia undistinguishable, except by its mode of causation, from progressive pernicious anæmia, resulted from a prolonged drain of blood from the uterus, there is no reason to suppose that the liver would contain an excess of iron pigment.

Hunter, if I understand him aright, would exclude from the category of pernicious anæmia, all cases of anæmia in which there is no excess of iron in the liver or kidney. But further information is wanted on this point. My belief is that in some cases in which all the clinical characteristics of pernicious anæmia are present during life, there is no excess of iron in the liver. Dr. W. B. Ransom brought before the Medical Section of the British Medical Association in August last a case of this kind. And even if Hunter's view (that pernicious anæmia is a separate and distinct clinical entity) is correct, the clinical physician would still be left in doubt and perplexity as regards the diagnosis of some cases during life; for, if I understand him correctly, Hunter regards the condition of the liver, in respect to the presence or absence of an excess of iron, as the most easily recognised evidence of the increased destruction which is the characteristic of the disease. He considers that those cases of anæmia in which the liver contains a great excess of iron are cases of pernicious anæmia; but that those cases in which there is no excess of iron in the liver are not. But even if this point is granted—and for the reasons given above I am not as yet prepared to grant it—the condition of the liver is a change which cannot be determined during life; unless the new photography can demonstrate its presence. In short, it is, I think, premature to conclude that a profound anæmia which proves fatal and in which there is no excess of iron in the liver, is never pernicious.

I doubt, too, whether we can absolutely rely upon the condition of the urine as a clinical test of pernicious anæmia. So far as my experience enables me to judge, a highly pigmented condition of the urine is not invariably present; and in those

cases in which it is observed, it may be merely temporary and evanescent.

Further, if we admit that a condition undistinguishable during life from pernicious anæmia may be the result of long-continued hæmorrhage, we must further, I think, allow that it probably may also be due to long-continued diarrhœa and perhaps to other conditions. Again, it seems certain that a condition closely resembling, and in some cases apparently identical with, pernicious anæmia may be the result of intestinal parasites. Further, there seems reason to suppose that in some cases which commence as chlorosis, a condition of pernicious anæmia is ultimately established.

In the present state of our knowledge, then, I am disposed to think :—

(1) That pernicious anæmia should be regarded as a clinical condition which may result from a variety of causes rather than one definite and distinct disease, in other words, that the term pernicious anæmia should be applied to any profound and apparently causeless anæmia characterised by the blood alterations which I have described above, and in which the anæmia tends to pursue a progressive or pernicious course.

(2) That the clinical condition, pernicious anæmia, may be the result either of excessive blood destruction or of defective blood formation

(3) That in many of the most typical cases of pernicious anæmia the two conditions (excessive destruction and defective formation) are combined.

(4) That in those cases in which the condition is due to excessive blood destruction, the blood destruction may be due to a variety of different causes and conditions. It is probable, I think, that pernicious anæmia is usually, as Dr Hunter has shown, the result of the increased blood destruction in the portal circulation due to the absorption of some poisonous substance from the gastro-intestinal tract, that in others a form of anæmia which is clinically (during life) undistinguishable from this (the Hunterian) type of pernicious anæmia, is the result of a long-continued drain of blood from the intestine (as in cases of ankylostomum duodenale), from the uterus, or in the case to which I have previously referred, that in others it is perhaps due to long-continued diarrhœa, and that in some cases it is perhaps developed on the top so to speak of the malarial, syphilitic and cancerous cachexia.

(5) That the condition is in some cases probably due to primary changes in the bone marrow and is therefore the result of defective blood formation.

Before we can come to a definite conclusion regarding the exact nature and causation of pernicious anæmia, it is essential to determine (1) whether the excess of iron in the liver which Hunter and others have described is invariably present in all fatal cases in which the clinical group of symptoms characteristic of pernicious anæmia was present during life; and (2) whether such an excess of iron in the liver is necessarily indicative of excessive blood destruction in the portal circulation alone. It is only after these questions have been decided by a sufficiently wide series of observations that it will be possible to determine whether the condition which we term pernicious anæmia is a definite disease which is always the result of blood destruction in the portal circulation, or whether it may not be, as I suppose, the ultimate clinical result of a number of different pathological conditions. The solution of this question is of great importance both for the purpose of diagnosis, prognosis and treatment.

Diagnosis.—In well-marked cases of pernicious anæmia, the diagnosis does not, as a rule, present any difficulty. The clinical features which are most important for the purposes of diagnosis are :—

1. The insidious development and progressive course, unless of course the disease is arrested and cured by treatment.

2. The great diminution of red blood corpuscles.

3. The comparatively small diminution of hæmoglobin and the consequent fact that the individual red blood corpuscles contain at least the normal amount, and usually more than the normal amount, of hæmoglobin.

4. The marked alterations in size and shape which the red blood corpuscles present, and especially the presence of the small red microcytes described by Eichhorst.

5. The retinal hæmorrhages.

6. The inutility of iron and the beneficial effect of arsenic.

I attach less importance to this point than I did some years ago, for in some recent cases of pernicious anæmia remarkable benefit has speedily been established under the combined use of iron in the form of Robertson's capsules, and large doses of liquor arsenicalis. I think it probable that the arsenic was the active agent which produced the improvement, but I am not prepared to say that the iron may not also have been beneficial. Indeed, a few cases have been recorded by other observers which were apparently cases of pernicious anæmia and in which marked improvement occurred under the administration of iron. But speaking generally, the therapeutic effect of iron on the one hand and of arsenic on the other is undoubtedly helpful for the purposes of diagnosis. It is certain, I think, that in most cases of pernicious anæmia iron is useless or even harmful; whereas in most cases (provided they are seen sufficiently early and the patient can take sufficiently large doses of the remedy) arsenic does good.

7. The occurrence of febrile attacks, apparently due to the anæmic condition, and independent of any other cause.

8. The presence of dark-coloured urine. As I have already stated, excessive pigmentation of the urine is often absent; and when present is usually only temporary and associated with fever and the paroxysmal exacerbations of the symptoms which are so characteristic of the disease. Nevertheless I agree with Dr. Hunter in thinking that the occurrence of highly pigmented urine in any case of profound anæmia is of considerable diagnostic significance. He says :—

'In addition to this, their pathological significance, these changes are, I am inclined to think, of no little importance from a diagnostic point of view. The high colour of the urine observed, unaccompanied as it was by any diminution in quantity or any rise in specific gravity, and the presence of granules of blood-pigment in the urine, pointed so unmistakably to the nature of the pathological process at work in the blood, that they establish conclusively the diagnosis of the case as one of pernicious anæmia.

'One must, however, in this connexion guard one's-self against a misconception that may not improbably arise. The urine in pernicious anæmia need not *always* show these well-marked and, when present, characteristic changes. It may be said however, with some degree of assurance, that they will be found more or less marked in all cases at some period or other of their history.

'In all cases, as in the foregoing one, there will be times corresponding to the periods when the patient is gaining ground, when the colour of the urine will be that of health, and nothing abnormal will be microscopically recognisable.

'The aggravations of weakness will always, however, be evidenced by a higher colour of the urine, it may be also by the appearance of blood-pigment granules in the urine; both

changes marking the nature of the process within the blood which is the occasion of these attacks, namely excessive hæmolysis.'

9. The absence of local or visceral disease capable of accounting for the anæmia. This is of course an important diagnostic point. Pernicious anæmia is, as we have seen, one of the primary forms of anæmia, although in some cases the group of clinical symptoms indicative of pernicious anæmia appear to be associated with, or developed secondarily to, cancer of the stomach, the presence of parasites in the stools, and perhaps with some other forms of visceral lesion.

10. The age and sex of the patient. These are in some cases of considerable diagnostic value, more particularly in determining whether a profound anæmia is the result of chlorosis or pernicious anæmia.

The differential diagnosis of chlorosis and pernicious anæmia.—I have already considered this point in connection with chlorosis. The distinction must, as I have previously stated, be chiefly based upon:—(a) The condition of the blood; (b) the presence of retinal hæmorrhages; (c) the therapeutic effect of iron on the one hand and of arsenic on the other; and (d) the age and sex of the patient.

The difficulty of distinguishing pernicious anæmia and chlorosis is only likely to occur in those exceptional cases of pernicious anæmia which occur in women at the time when chlorosis is most frequently developed, and in those exceptional cases of chlorosis in which the patient in no longer a young woman, and in which the patient is a male or a child. Pernicious anæmia rarely occurs in young women, whereas chlorosis is essentially a disease of young women. It must further be remembered that pernicious anæmia, as we have seen, is exceedingly rare in children.

The differential diagnosis of pernicious anæmia and primary heart disease.—This can rarely give rise to any difficulty. The same points which are important in distinguishing chlorosis and primary heart disease are of importance here, together with the condition of the blood and the fact that the cardiac symptoms were developed after the anæmia.

The differential diagnosis of pernicious anæmia and cancer of the stomach.—In some cases of cancer of the stomach in which there is no discoverable tumour, and especially in those cases in which the body of the stomach is involved, the orifices being free, the symptoms may closely resemble those of pernicious anæmia.

In both conditions there is progressive asthenia, anæmia and more or less emaciation, without, perhaps, any definite and discoverable cause.

In the great majority of cases the differential diagnosis can be satisfactorily arrived at by a judicial survey of the whole symptoms and physical signs of the case. The age of the patient, the severity of the stomach symptoms, the condition of the blood, the presence or absence of tenderness on pressure over the region of the stomach, of hæmatemesis, and especially of a tumour or localised hardness in the epigastric region or of difficulty in swallowing due to obstruction at the lower end of the œsophagus, are the most important points to which attention should be directed in doubtful cases.

The occurrence of hæmatemesis is strongly in favour of cancer, for in my experience bleeding from the stomach is extremely rare in cases of pernicious anæmia.

The differential diagnosis of pernicious anæmia and of Bright's disease.—There is rarely if ever any difficulty in distinguishing these conditions. The diagnosis of course turns upon the condition of the urine (presence of albumin, casts, etc.) on the one hand, and the condition of the blood (the presence of the alterations characteristic of pernicious anæmia) on the other.

The differential diagnosis of pernicious anæmia and splenic leukæmia.—This presents no difficulty. The two conditions are at once distinguished by the microscopical characters of the blood and the marked enlargement of the spleen.

The differential diagnosis of pernicious anæmia and splenic anæmia without leucocytosis.—In some cases in which the spleen is enlarged, there is profound anæmia but no increase of the white blood corpuscles. This form of anæmia is extremely rare; no case has come under my own observation. The essential points of distinction from pernicious anæmia are the enlargement of the spleen, which can, of course, be distinguished during life, and the characters of the blood—(a) the hæmoglobin appears to be diminished more than the corpuscles, in other words the anæmia is of the chlorotic rather than of the pernicious type; and (b) the red corpuscles do not (usually) present the extreme variations in size and shape which are characteristic of pernicious anæmia.

The differential diagnosis of pernicious anæmia and of medullary anæmia.—In considering the etiology and pathology of pernicious anæmia, we have seen that there is reason to suppose that in cases of pernicious anæmia of long standing, changes are apt to be produced in the medulla of the bones; and it seems probable that a form of anæmia presenting all the clinical characteristics of pernicious anæmia may in rare instances result from a primary lesion of the bone marrow. I know of no means by which such a condition can be distinguished from the usual (Hunterian) type of pernicious anæmia during life, except by the presence of swelling and tenderness over the bones and sternum, and it is doubtful whether such swelling and tenderness are always and necessarily present. Whether in such cases the liver contains an excess of iron or not is, as I have already pointed out, a matter which requires to be determined by future observation. It is one of the facts which require to be settled before we can come to a definite conclusion as to whether the condition which we term pernicious anæmia is a definite and distinct disease, or whether it is a clinical condition which may result from a variety of morbid lesions.

Prognosis.—The prognosis of pernicious anæmia is always very grave. In many cases the disease steadily progresses in spite of treatment, and the great majority of cases ultimately terminate in death. Until I introduced the arsenic plan of treatment, no method of treatment seemed to produce any beneficial effect upon the course of the disease. The opinion expressed by Addison practically represented the experience of all clinical observers. Under arsenical treatment, the prognosis is certainly more hopeful. No one who has had large experience of the disease and has given the arsenic a fair chance can fail, I think, to come to the conclusion that some cases improve in the most remarkable way under the steady administration of the drug. In some cases the improvement is so rapid and remarkable that, in them, arsenic seems almost to be a specific. In other cases, the administration of arsenic appears to produce little or no benefit. In the great majority of the cases which are temporarily relieved and it may be for the time apparently cured by arsenic, a relapse subsequently occurs, and in many cases the relapse proves fatal. Several instances of this kind

have come under my own observation. A tendency to relapse is one of the most striking features of the disease, and in this respect pernicious anæmia closely resembles chlorosis. It remains to be seen whether relapses can be prevented by the continued administration of arsenic or of bone marrow; for, as I shall presently point out, there is some reason to suppose that bone marrow is in certain cases an effective agent in the treatment of the disease. It is, I think, reasonable to hope that in some cases at all events, relapses may be prevented by the continued administration of small doses of arsenic or of bone marrow, in addition to minute attention to the general health, to the hygienic surroundings, and to the condition of the gastro-intestinal tract.

The prognosis of course largely depends upon the degree of anæmia which is present. The disease is almost always fatal in cases in which the number of blood corpuscles sinks below 600,000 per cubic millimetre.

The duration of the disease is also an important point so far as the prognosis is concerned, for in the later stages of the disease arsenic is often apparently useless; but this is by no means always the case.

The prognosis is, perhaps, more unfavourable in young subjects than in middle-aged adults; but I speak with uncertainty on this point.

The prognosis is always very grave in those cases in which epistaxis, bleeding from the gums, or other external hæmorrhages occur. The presence of obstinate and intractable diarrhœa is always unfavourable. Profound nervous symptoms, restlessness, delirium, semi-coma, convulsions, or coma are most unfavourable indications; they are usually only developed just before death.

In estimating the chances of recovery in any given case, the degree of the anæmia, the length of time which the disease has continued, the age of the patient, his ability to take arsenic in large doses for long periods of time, and the presence or absence of complications, such as an ulcerated condition of the intestine, are I think the most important points. Most of the cases of pernicious anæmia which have come under my observation of recent years have proved rapidly fatal; but almost all of them have been seen at the very terminal period of the disease. In cases of this kind the arsenical plan of treatment has little or no chance. The stage of the disease and its duration are in my opinion most important points so far as the prognosis is concerned. Provided that the case is not too far advanced and that it is not of too long duration, there is in many cases a reasonable hope of improvement, provided only that large doses of arsenic can be borne.

Treatment.—Up to the time I introduced the administration of arsenic, pernicious anæmia was almost always, I think I may say invariably, fatal. Since that time remarkable improvement and apparent cure, which unfortunately is usually only temporary, has resulted in many cases. It may, I think, be confidently stated that the value of the arsenic treatment has been definitely established by numerous independent observers. Dr. Padley, Dr. Pye-Smith and Dr. Lockie in this country have published a series of cases which show the beneficial effects of arsenic.

I was led to try the administration of arsenic in pernicious anæmia by the following reason:—I knew from my pathological observation that in cases of pernicious anæmia the most striking naked eye appearance was the extreme fatty degeneration of the heart. I further knew that arsenic was a remedy of undoubted value in the treatment of many cases of fatty heart. I said to myself, Why not try the effect of arsenic in pernicious anæmia? I happened at the time to have a run of cases of pernicious anæmia under my care in the Newcastle Infirmary. In the first case in which I tried the remedy, rapid and immediate improvement took place, and in two others the same result was also obtained. Since coming to Edinburgh, I have not had the opportunity of treating a single case of pernicious anæmia in hospital practice, and since Dr. Hunter's observations were published I have only had post mortems.[1] The cases that I have seen have all occurred in private (consulting) practice. In several of these cases very marked and rapid improvement has taken place under arsenic; but the great majority died before sufficient time had elapsed for improvement to take place under arsenic or any other plan of treatment. In fact, most of the cases which have come under my notice of recent years were seen once in consultation a few days only before the fatal termination took place.

Before referring to the dose of arsenic and the mode of administration, let me say a few words with regard to the general treatment of the disease; for in this form of anæmia, as in chlorosis, attention to the hygienic surroundings and the feeding of the patient are of great importance.

It is essential, I think, when the anæmia is at all marked, that the patient should be kept in bed, or at all events in the recumbent position.

The patient should have plenty of fresh air, and if possible an abundance of sunlight.

The diet should be light and nutritious. Owing to the impaired digestive power of the stomach, the patient is usually unable to digest solid food. Milk and milk foods, meat extracts (of which Wyeth's is perhaps the best), raw beef juice, finely grated and pounded raw meat and whipped-up eggs should form the basis of the dietary. On the view that pernicious anæmia is the result of blood destruction in the portal circulation and that there is an excess of iron in the blood, a milk diet would theoretically be preferable to a red meat diet; but I have not been able to satisfy myself from my own observation that the administration of meat extracts, beef juice, or pounded raw meat is in any way harmful. On the contrary, I am disposed to think that a meat diet is in many cases beneficial.

In administering arsenic, I usually begin with a small dose—two drops of Fowler's solution three times a day, given in plenty of water soon after food. I gradually increase the dose by one drop every second day, so that on the third day the patient is taking three drops, and so on. Many patients affected with pernicious anæmia can ultimately take ten, fifteen, or even twenty drops of Fowler's solution three times daily. The object of the treatment is to gradually increase the dose until the maximum quantity that the patient can take without any discomfort is reached. When the patient begins to complain of itching of the eyeballs, pain in the stomach or diarrhœa, the dose should be immediately and considerably reduced; subsequently it may again be increased and the remedy continued in the largest dose which can be comfortably and satisfactorily borne. The long-continued administration of arsenic in some cases produces pigmentation of the skin. I have not myself observed this effect in any case of pernicious

[1] Since this article was written a typical case has been admitted (October 1896) into my Ward in the Edinburgh Royal Infirmary.

anæmia, though I have in several other diseased conditions. Many patients who are suffering from pernicious anæmia seem to have a tolerance for the drug. The same thing is seen in many other diseases in which a remedy is markedly beneficial; for example, iodide of potassium in syphilis, opium in peritonitis, iron in chlorosis, and chloral hydrate in some cases of nervous spasm, etc.

In those cases in which the arsenic agrees and is attended with benefit, it should be steadily continued in full doses until the number of red blood corpuscles comes up to the normal and until the symptoms of the disease disappear. When the patient is apparently cured, the dose should be reduced, but the remedy should still be given in small doses—two or three drops of Fowler's solution three times a day. I am of opinion that these small doses should be continued for several months at least, and probably, if relapses are to be prevented, for several years. I am hopeful that if this plan of treatment is systematically carried out, relapses will in future be found to be less common than they have been in the past.

The exact manner in which arsenic produces its beneficial effects in pernicious anæmia is not yet determined. Dr. Hunter suggests that it probably acts by producing a healthier condition of the gastro-intestinal tract, that is to say by preventing the formation and absorption of the toxic products which he thinks are the essential causes of the disease. Dr. Copeman has shown that under the administration of arsenic in pernicious anæmia, the hæmoglobin is much more stable; it does not tend to separate from the corpuscles after withdrawal from the body in the way which it does before the arsenic is administered. It is probable, I think, that the remedy acts as a blood tonic and that it exerts a beneficial effect upon the bone marrow, enabling the marrow to form healthier red blood corpuscles—blood corpuscles in which the hæmoglobin is more stable and more intimately combined. But be this as it may, the beneficial effect of the remedy in many cases of the disease is definitely established.

The condition of the bowels must be carefully regulated. If there is constipation, gentle laxatives should be given; aloin, cascara and sulphur are probably the best. If there is diarrhœa, it should be arrested as soon as possible; salicylate of bismuth is one of the best remedies for this purpose. When there is reason to suppose that decomposition is going on in the intestine, intestinal antiseptics may be tried. Beta naphthol, thymol, menthol and salol have been recommended for this purpose. Thymol, one grain three times a day, is probably the most effective.

Believing that the disease is due to the absorption of a poison from the intestines, Dr. Hunter has recommended the administration of intestinal antiseptics, e.g. salol or Beta naphthol; Dr. George Gibson has published a case in which this plan of treatment seemed to produce a remarkably beneficial effect. In the only two cases in which I have tried it, there was no improvement.

If there is reason to suspect the presence of intestinal worms (and in all cases of pernicious anæmia the fæces should be examined for ova, parasites, etc.), such remedies as thymol or santonin should be given.

It is unnecessary to say that in those cases in which the patient is losing blood from the uterus, piles, etc., the hæmorrhage should be arrested as speedily as possible.

In rickety or syphilitic children who are suffering from profound anæmia, the appropriate treatment for rickets is of course essential and arsenic and iron may at the same time be given. These cases can hardly, however, be included under the term pernicious anæmia, though the blood condition is very similar, so far at all events as the shape and size of the red blood corpuscles are concerned.

In most cases of true pernicious anæmia, iron usually fails to produce any beneficial effect; indeed, in some cases it seems to be prejudicial. But, as I have already stated, I speak with less confidence on this point than I did some years ago, for in some of my recent cases most marked improvement has occurred under the simultaneous administration of Robertson's capsules and of large and gradually increasing doses of arsenic. The improvement in two of these cases was so marked that I now feel it a duty to prescribe the same combination—iron and arsenic—but the effect of the iron on the disease should be carefully watched; in a recent case the patient himself volunteered the statement that it did harm rather than good.

Oxygen inhalations have also been recommended, and in any future case which comes under my own observation, in hospital practice at least, where the effects of the treatment can be closely watched and where the remedy can be assiduously given, I intend to try oxygen inhalations.

Professor Fraser has recommended the administration of bone marrow, and has published a case in which remarkable improvement occurred under the combined administration of bone marrow and arsenic. He concluded that the improvement was due to the bone marrow rather than the arsenic. It remains to be seen whether further observation will confirm this opinion or not; and it is only fair to state that (I am informed) in that case, as in so many other cases of pernicious anæmia, the disease relapsed and the patient died some little time after his discharge from hospital.

So far as present experience enables us to judge, bone marrow appears to be a much less efficacious remedy than arsenic. Further information is required before it is possible to pronounce a positive opinion as to its value in pernicious anæmia; but if I am correct in supposing that in many cases of the disease the destruction of the red blood corpuscles in the portal circulation results in the production of functional and perhaps structural changes in the bone marrow, the administration of bone marrow seems indicated on theoretical grounds.

Further, if progressive pernicious anæmia is a clinical result of several different conditions, it is not unreasonable to hope that further observation and experience will enable us to differentiate the cases in which arsenic (and possibly bone marrow) are most beneficial.

I can only repeat that in the advanced stages of grave cases it is unreasonable to expect improvement under any of our present plans of treatment.

Transfusion of blood or saline solution has been tried by various observers. In the great majority of cases the effect was negative or prejudicial. From the results obtained in his experimental observations on the lower animals, Dr. Hunter is strongly disposed to think that transfusion will be likely to do more harm than good. The only possible effect which, in his opinion, it is likely to produce is temporary benefit. But notwithstanding his theoretical objections, which seem to be based on satisfactory reasoning, good results have undoubtedly been obtained in a few cases. A remarkable illustration in point was published by Dr. Affleck a few years ago. In three cases, too, published by the late Dr. Brakenridge, in which

repeated transfusion of small quantities of blood was practised, the result was very satisfactory. In one of my cases (a private patient) in which blood transfusion by the direct method was practised by Mr. Cotterill, a temporary rally took place, but the patient died very shortly after the operation.

The intra-venous injection of milk has also been recommended, but, so far as I know, has never been shown to produce any beneficial effect.

Cases of pernicious anæmia which have been temporarily cured by arsenic should be closely and continuously watched. The blood should be examined from time to time. If any indications of a relapse develop, the patient should immediately be placed under treatment.

NOTE.—*The new photography in the diagnosis of pernicious anæmia.* At a recent clinique in the Edinburgh Royal Infirmary a student suggested that it might be possible to detect the excess of iron which is present in the liver in cases of pernicious anæmia by means of the X rays. The suggestion is a valuable one. Dr. Dawson Turner kindly took a photograph for me in a case which I have at present under observation. A well-marked shadow of the liver was obtained, but Dr. Turner was unable to say that it was abnormally deep and dark. The result in this case is therefore negative, but the subject deserves further investigation.

NOTES OF CASES OF PERNICIOUS ANÆMIA TREATED WITH ARSENIC.

I append to this article a record of the cases of pernicious anæmia in which I originally employed the arsenical plan of treatment. The paper was published in the *Edinburgh Medical Journal*, 18th November 1877.

Case I. Profound Anæmia following Yellow Fever. Vomiting. Diarrhœa. Irregular Elevations of Temperature. Marked Alterations in the Microscopical Characters of the Blood. Retinal Hæmorrhages. Recovery.

Alfred Rush, æt. 20, a foreign sailor, was admitted to the Newcastle Infirmary under my care on the 21st March 1875, suffering from profound anæmia.

Previous History.—He was quite well until four and a half months ago, when he was attacked with yellow fever. He was laid up with the disease for six weeks. After getting better he caught cold, and has been ill since. He came into the Tyne about Christmas, and was at once admitted to the floating hospital under the care of my brother, Dr. J. W. Bramwell. His feet and legs have been swollen. He has had a slight cough, has frequently vomited, and has been every now and again confined to bed with irregular attacks of fever. He has had several attacks of epistaxis, and has been frequently severely purged. He has taken large quantities of iron and quinine, together with the mineral acids and a liberal diet. In spite of all treatment he is no better. He has not had syphilis.

Condition on Admission.—He is tall and fair; hair of a light-brown colour. His face looks slightly puffy about the eyelids, and is of a pale lemon hue; the skin is smooth and waxy; the lips and mucous membranes are very anæmic. The conjunctivæ are slightly yellow, and there is a small yellow deposit of fat at each inner canthus. The pupils are dilated, but readily contract in the stimulus of light. The feet are not now œdematous.

Alimentary System.—The tongue is clean, smooth, pale, moist, and slightly flabby; the appetite is poor; there is considerable thirst; he frequently vomits. The vomited matters are sometimes green, sometimes yellow. The bowels are regular, the motion light-coloured and semi-solid.

The abdomen is flaccid and tympanitic on percussion. The splenic dulness is sometimes increased. The size of the liver is normal.

Circulating System.—The heart is of normal size. A soft systolic murmur is audible all over the cardiac area, its point of maximum intensity being the apex. The radial pulse numbers 112; it is visible, very weak, easily compressible, and has a slight thrill.

Respiratory System.—He complains of soreness on taking a full breath. A few sibilant and sonorous râles are heard over both lungs. There is no cough nor spit.

Urinary System.—The urine is very pale, sp. g. 1017. It contains no albumen.

Nervous System.—He complains of headache. The nervous system is otherwise normal. On ophthalmoscopic examination the discs are found to be normal.

The temperature is 99° F.

A drop of blood drawn from the finger in the usual way was found to be thin and watery. It speedily separated into two parts, one coloured, the other colourless, looking as if a drop of colourless oil had been added to a red liquid. On microscopical examination it presented the following characters:—The red globules were diminished in numbers, and did not form rouleaux. They were markedly altered in shape, some of them being large, and no longer biconcave; others irregular, and with one or more tail-like projections; others appeared nucleated; the nucleus was of a pinkish-red colour. There were also numerous small red globules; indeed, they (the red globules) seemed to be of all sizes, from minute masses of protoplasm to the abnormally large oval corpuscles which I have described. (A coloured plate illustrative of these appearances was published in the original paper.) The white corpuscles were not increased. In addition there were many small colourless granules; some of these formed irregular masses, somewhat larger than white blood corpuscles. In one specimen an emerald green rod-shaped body about $\frac{1}{1000}$th of an inch in length was observed: it seemed to move with a slight vibratile movement. Nothing of the sort was again observed; its occurrence was therefore probably accidental.

Treatment.—He was ordered twenty drops of the tincture of the muriate of iron three times a day.

Subsequent Progress of the Case.—*On 22nd March* he was not so well, having vomited several times through the night.

On 23rd March he was still worse. The evening temperature was 105° F. The iron was discontinued, and a febrifuge mixture substituted. He complained of pain and tenderness on pressure about the umbilicus.

On 24th March he complained of dimness of vision. On ophthalmoscopic examination several hæmorrhages were seen in both retinæ, most marked in the right.

On 25th March he was better, though still vomiting. Milk diet was ordered, and two drops of liquor arsenicalis thrice daily prescribed.

On 2nd April he was decidedly better. The arsenic was increased to four drops. Beef tea and chicken broth were added to the diet.

On 13th April he was still better. An ounce of lime juice was ordered.

On 28th April he was greatly improved. The retinal hæmorrhages were still visible. The improvement gradually continued. He was sent to the Convalescent Home at Whitley on 17th June.

Remarks.—The profound anæmia occurring without any obvious cause, and associated with the characters of the blood and the retinal hæmorrhages which I have described, was a combination of symptoms which had not before come under my notice. I confess I was as completely puzzled as my brother had been.

On 10th June another case similar in all respects was admitted under my care, and died on 28th June. The post-mortem revealed

nothing of importance. I was still as much in the dark as ever.

Soon after this date my friend Dr. Beatson, our then house surgeon, mentioned my difficulties to Professor Grainger Stewart, of Edinburgh, who at once recognised the true nature of the case, and referred me to the authorities I have already quoted.

I thus found that the retinal hæmorrhages which I had observed had been previously described by Dr. Biermer and others.

The peculiar condition of the blood had also been independently noted. The observations of Professor Eichhorst of Jena were published in the *Centralblatt Med. Wiss.*, No. 26, 1876, and are thus translated in a note which appeared at the end of a clinical lecture by Professor Quincke of Berne, published in the *Medical Times and Gazette*, 14th October 1876:—'He asserts that a constant alteration of the red blood globules can always be detected. While a portion retain their normal size, and are only distinguished by their remarkable paleness and slight tendency to form rouleaux, the remainder immediately attract attention by their diminished size. Their diameter may scarcely be a quarter of a healthy corpuscle, while their colour is of a deeper red than normal, and when seen in profile they seem to have more or less completely lost their biconcave outline. Their size may be even so much diminished that many of them resemble small red-tinted fat drops. The alteration here described has not been detected in anæmic and cachectic conditions other than pernicious anæmia. The white corpuscles were present in all the cases observed (seven in number) in remarkably small proportions.'

This description tallies remarkably with my own. In many of my cases some of the red globules were apparently nucleated, others were not more than a quarter the size of a healthy corpuscle. I failed to observe that they, *i.e.* the small red globules, were of a deeper red than normal. Those small red globules which were apparently nucleated certainly had the appearance Professor Eichhorst describes; but only a few of them were nucleated. The small red globules which were not nucleated were of a very pale yellow colour, in fact, of the same colour as the large red globules. In one case which was fatal, numerous small emerald-green molecules were seen; these were probably not of much consequence, for I have noted their presence, though never in the same number, in other diseases.

In the clinical lecture to which this note was appended, Professor Quincke states that in his cases the red globules were diminished in number, and altered in shape and size. Some of them were smaller than normal, and amongst them were a number of tiny yellowish particles. In several cases, he says, 'those finely granular masses which are sometimes lustreless and sometimes shining, and which are common in the blood of cachectic individuals, were found in great abundance.' In his eighth case they were so abundant that they rendered the serum of the blood cloudy. This cloudy appearance was not present in any of my cases.

I have detailed the microscopical characters of the blood at length, for they are of great diagnostic value. The nucleated appearance which some of the red globules presented has not, I think, been before observed. Until quite recently, I was inclined to think the nucleation only apparent, and produced by an indentation or curving in of the corpuscle at one point. Most of the nucleated corpuscles were so indented. The appearance may, however, be of more importance than I at first supposed.[1]

Case II. Profound Causeless Anæmia. Skin smooth and ivory-like, of a slight yellow tinge. Hair prematurely grey. Red Blood Corpuscles diminished in number, and of all shapes and sizes, many of them apparently nucleated. Numerous retinal Hæmorrhages. Vomiting. Great Restlessness. Delirium. High Temperature. Death. Post-mortem Appearances:—Bloodless Condition of Body. Fatty Degeneration of Heart, Aorta, Liver, Kidneys. Small Calcareous Deposit in Mitral Valve. Enlargement of Spleen and Thyroid. Mammillated Appearance of Stomach.

John H., æt. 34, grocer's assistant, single, living at Houghton-le-Spring, Durham, was admitted on 10th June 1875, complaining of great general weakness.

[1] This apparent nucleation has been explained by Messrs Mackeyn and Davy. It is due, they say,—and, I believe, correctly,—to the separation of the hæmoglobin from the stroma.—*Lancet*, 5th May 1877.

Previous History.—Has never been very strong, but was never laid up. His present illness commenced two years ago, with loss of strength. He noticed at the same time that he was getting paler and paler. He has not had syphilis, nor any exhausting discharge. Has had a comfortable dry home. He never had intermittent fever. For the last few months he has been very much worse. His feet and ankles have swelled. He has occasionally vomited. Has drunk beer to excess for fifteen years. He knows no cause for his present illness.

Family History.—Particularly good.

State on Admission.—He is too weak to walk. Whenever he sits up he feels giddy and faint. The face has a pale yellow tinge, and is slightly swollen. He is profoundly anæmic. The skin has a yellowish-white glistening appearance. The hair is grey; it used to be black; the eyebrows are dark and bushy. The pupils are moderately dilated, and very sensitive to light. Ophthalmoscopic examination is difficult owing to the fact that whenever the light is thrown into the eye, the patient moves his head to one side, or shuts his eyes. After dilatation with atropia, a good view was obtained, and the retinæ were seen to be spotted with numerous extravasations. Sight, he said, was good, and always had been so. The vessels of the disc were so bloodless as to be almost invisible. Some of the veins of the retina were congested in the form of streaks. The hæmorrhages were chiefly in the course of the vessels.

The feet are slightly œdematous. The patient is thin, the muscles being soft and wasted; muscular irritability is very marked.

Alimentary System.—The lips and gums are highly anæmic. The tongue is very pale, clean and moist; the appetite poor. He occasionally vomits, but not at any particular time. The vomited matters are green or yellow, and very bitter. The bowels are costive. For the last four months he has been troubled with internal piles, but has only once passed a little blood. The liver dulness measures 5 inches; the splenic dulness is somewhat increased.

The blood presents the same characters, but even more marked than in the previous case, the red globules being greatly diminished in number, and of all shapes and sizes. Many of them are apparently nucleated. The white corpuscles are few; some of them small, others large and oval.

Circulatory System.—The cardiac dulness is somewhat increased; transversely it extends from the left border of the sternum to the nipple. The heart's action is uncertain, and somewhat tumultuous. There is a well-marked apex systolic murmur. The pulmonary sounds are louder than the aortic; a loud venous hum is heard on both sides of the neck. The external jugular veins are distended and knotted, but not pulsating. The radial pulse is very weak: irregular, with a slight thrill. It numbers 100 in the minute.

The Respiratory Organs are natural.

The Urine is natural.

He is very restless, tossing about in bed. Sleep is disturbed and fitful.

Treatment.—A grain of quinine three times daily, with milk and beef-tea *ad libitum*, were prescribed.

Subsequent Progress of the Case.—In the first few days after admission, he remained *in statu quo*.

On 17*th June* he was ordered twenty drops of the tincture of the muriate of iron.

On 18*th June* he was much worse, constantly tossing about in bed, and complaining of thirst; the tongue was moist. The temperature was 102·6° F.

On 19*th June* he was still worse. Had passed a very bad night. He complained of aching pains in the legs, and of a choking feeling in the throat. The thyroid was found to be considerably enlarged. This had not been previously observed. The iron was discontinued; half an ounce of lemon juice was ordered, and the dose of quinine increased to two grains.

On 21*st June* he was rather better; the temperature and pulse had fallen; he had twice vomited. Two ounces of brandy were added to the diet.

On 23*rd June* he was very much worse; the face had a sunken expression.

On 24*th June* he was very restless and delirious; he had tossed about all night, and 'worked with his fingers about his neck,' saying there was something there which was choking him.

On 25*th June* he died at 10.40 A.M. The temperature rose rapidly before death. The highest point observed was 105° F. (see fig. 16.) I took the temperature at 12 noon (an hour and twenty minutes after death); it was then 102°·8 F.

Autopsy (four hours after death).—*External Appearances.*—The body was warm; skin of a pale yellow hue; feet and legs œdematous. The abdominal parietes contained a fair amount of fat.

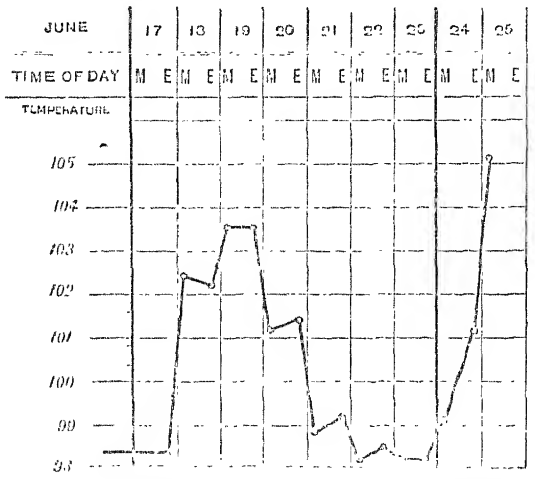

FIG. 16.—Temperature chart in the case of John H. (Pernicious Anæmia ending fatally).

Thorax.—The *Pericardium* contained a few ounces of yellow serum. The *Heart* weighed 13½ ounces, and was covered with fat. On the interior wall of the right ventricle, just over the position of the tricuspid valve, there was a large milk spot; another smaller one was situated on the anterior aspect of the apex. On the anterior surface of the left ventricle, half an inch above the apex, there was an extravasation of blood as big as a threepenny piece. The cavities of the organ were almost empty, the only contents being about three teaspoonfuls of thin fluid blood. The posterior segment of the mitral valve contained a small calcareous deposit, and was somewhat shrunken. The cavities were dilated; the muscular substance very soft and friable. The interior of the left ventricle, especially the papillary muscles, was dotted with little spots of fatty degeneration. The interior of the aorta was spotted here and there in a similar manner. Under the microscope the cardiac muscle was seen to be decidedly fatty.

Lungs.—The left was pale and completely bloodless; its weight 9¼ ounces. The right was slightly adherent at the apex; it weighed 1 lb. 4¼ ounces. There was a commencing consolidation at the posterior part of the upper lobe. On section of this part, a considerable quantity of red serum escaped.

The Bronchial Glands were not enlarged.

The Thyroid was the size of a hen's egg; it weighed 2½ ounces. Both lobes were enlarged. On section, it was seen to be in places yellow and gelatinous, in others of a purple colour; at the lower part of the left lobe there was a calcareous mass. On microscopical examination the gland was found to be in a state of colloid degeneration. In parts there was calcareous infiltration.

The Liver weighed 4 lbs. ½ oz., and was fatty.

The Spleen weighed 9½ ounces, was of a uniform dark purple colour, and firm. On microscopical examination it seemed normal.

Kidneys.—The left weighed 7, the right 5½ ounces. Both were embedded in fat. The cortical substance was pale. On microscopical examination the renal epithelium was found to be in places fatty.

The Stomach in the neighbourhood of the pylorus was studded with small round projections. These projections were arranged in rows, and were found on microscopical examination to consist of round lymphoid cells. The mucous membrane of the *small intestine* seemed softened and atrophied. The various coats of the gut were more loosely connected than in health.

The Supra-renal Capsules and other organs were healthy.

The Post-mortem Appearances may be summed up as a bloodless condition of the body; fatty degeneration of the heart, aorta, liver, and kidneys; enlargement of the thyroid gland and spleen; a mammillated appearance of the stomach, and an atrophied condition of the intestine. The small calcareous deposit in the mitral valve was not of great moment. The condition of the right lung was quite recent, and had nothing to do with the essential pathology of the disease.

The bloodless condition of the body and the fatty degeneration have been observed in all cases. The enlargement of the spleen has also been previously noted. The enlargement of the thyroid has not, I think, been before seen; it was probably, therefore, an accidental complication. The mammillated appearance of the stomach is interesting. This condition sometimes occurs in Addison's disease, and is described by Dr. Greenhow (*Croonian Lectures*, 1875, p. 28).

I regret that the medulla of the bones was not examined. Professor Pepper of the University of Pennsylvania, who has written a very able paper on the subject,[1] was the first to describe an abnormal appearance of the marrow, and founded on it a theory as to the nature of the affection. He thinks progressive pernicious anæmia is simply the medullary form of pseudo-leukæmia. Since the appearance of Professor Pepper's paper the marrow has been examined by other observers. Some, as Dr. Bradbury of Cambridge, have failed to find anything abnormal; others, as Professor Cohnheim, have found marked changes. The constant occurrence, therefore, of the marrow lesion is still *sub judice*.

Case III. Profound Anæmia following an attack of Yellow Fever. Marked Alterations in the Red Blood Corpuscles. Retinal Hæmorrhages. Obstinate Diarrhœa. Anæmic Murmurs at Base of Heart and in Vessels of Neck. Giddiness and Faintness on Exertion. Death. Autopsy:—Bloodless Condition of Body. Fatty Degeneration of Heart and Liver. Œdema of left Leg. Slight Ulceration of Small Intestine at Ileo-Cæcal Valve.

F. N., æt. 28, a foreign sailor, was admitted on 16th August 1875, complaining of diarrhœa and great debility.

Previous History.—He had yellow fever seven months ago, and has been out of health since. The diarrhœa commenced a fortnight ago. Before the attack of yellow fever he was a healthy man. He has not had syphilis.

Present Condition.—He is thin, emaciated, and markedly anæmic. The skin has a slight yellow tinge. The conjunctivæ are perfectly pearly. There is slight œdema about the eyelids, but nowhere else. He is very weak—hardly able to walk across the room. Whenever he gets up he feels a 'swimming' in the head, and has on more than one occasion tumbled down. The blood presents the same appearances as in the two previous cases. On ophthalmoscopic examination, a few retinal hæmorrhages, of small size, are seen in both eyes. The discs and surrounding retinæ are markedly pale, the arteries being hardly distinguishable from the veins.

A soft, blowing, systolic murmur is audible at the base of the heart, and there is a loud venous hum in the veins of the neck. The pulse numbers 84, and is small and weak. The tongue was smooth, pale, and moist: the appetite good. He complains of constant thirst.

The abdomen is distended with flatus, and, in consequence, the exact limit of the hepatic and splenic dulness cannot be defined.

The Urine amounts to 59 ounces in the 24 hours. It is pale, slightly acid, sp. gr. 1008, and contains a trace of albumen. On microscopical examination of the deposit, which is scanty, a few squamous epithelial and pus cells are seen.

The Temperature is normal.

The other Systems and organs are normal.

Treatment.—He was ordered milk diet and an astringent mixture.

Subsequent Progress of the Case.—He was purged several times during the first twenty-four hours after admission. The motions were watery, light-coloured, very offensive, liquid, and frothy.

On 20th August the diarrhœa had ceased. The urine was free from albumen. Eight grains of quinine, thrice daily, were prescribed.

On 28th August he was again severely purged. The chalk mixture was again administered.

On 30th August he was very much worse. Eight ounces of brandy were prescribed.

On 31st August the diarrhœa had stopped; but he was still very sunk and prostrate.

On 1st September he died.

The Post-mortem was made ten hours after death. The body was considerably emaciated. Rigor mortis was strongly marked.

Heart.—The pericardium contained two ounces of clear yellow serum. There was a small milk spot on the anterior surface of the left ventricle. The cavities of the heart contained a small quantity of thin liquid blood. The segments of the aortic valve were

[1] *American Journal of Medical Sciences* for October 1875.

slightly thickened. The valve was competent. The muscular substance was mottled with spots of fatty degeneration, and was very friable. The heart weighed 10 ounces.

Lungs.—Both were adherent throughout, the adhesions being very firm and dense. The left lung weighed 1 lb. 11 oz. On section, it was œdematous—especially the lower lobe posteriorly. The right lung weighed 1 lb. 8 oz.: a small quantity of frothy serum escaped from its lower lobe.

The Liver weighed 3 lb. 12 oz., and was fatty.

The Spleen weighed 3½ ounces, and was normal.

The Stomach contained about a pint of yellow-ochre-coloured fluid, and was normal.

The Intestines contained a large quantity of yellow-ochre fluid, similar to that found in the stomach. The mucous coat was very easily stripped off, and seemed softened. At the ileo-cæcal valve there was a small superficial ulceration the size of a sixpence.

The Appendix Vermiformis contained a small concretion.

The Mesenteric Glands were somewhat enlarged.

The Kidneys.—Both weighed 6½ ounces. They were smooth, fatty, pale, and bloodless.

The Supra-renal Capsules were normal.

The Thyroid Gland was normal.

The Brain weighed 51½ ounces, and was normal.

The body throughout was almost bloodless. The *Blood*, where present, was thin and watery.

The *Marrow* of the bones was not examined.

Remarks.—It is etiologically important to note that this patient had had an attack of yellow fever, and that his illness dated therefrom. The same history was present in Case I., already related.

Case IV. Profound Anæmia, with Emaciation. Changes in Size and Form of Red Blood Globules. Numbness and Loss of Power in Hands and Feet. Intense Reflex Action in Lower Extremities. Great Improvement under Quinine and Arsenic.

Thomas R., æt. 43, single, a cabman, was admitted on 18th March 1875, complaining of weakness and inability to walk.

Previous History.—He enjoyed excellent health until three years ago, when he was laid up for some weeks with swelled feet and 'yellowness of the face.' The doctor who attended him said he had a liver complaint. After recovering from this illness he continued well until Christmas, when he caught cold while working in a wet drain. He felt weak and ill, but managed to walk until five weeks ago. He then felt a numbness and loss of power in both hands. This was followed by weakness in the legs and great difficulty in walking.

He has been a hard drinker of spirits. Twenty years ago he had a chancre, but no secondary symptoms.

Present Condition.—Patient, who is a big-made man, is sallow, thin, and emaciated. The skin is dry and wrinkled, the mucous membranes are markedly anæmic.

He has great difficulty in walking, and his gait is very peculiar. He takes very long strides, and throws out his legs in an uncertain manner. The back is kept slightly arched, the head thrown back, the arms extended, one on either side of him, the palms being directed backwards, the forefinger and thumb of each hand approximated. When in bed he can move the legs in any direction. The reflex movements, on tickling the soles of his feet, are intense. The contractility of the muscles to the electric current is diminished. There is marked loss of grasping power in both hands. He is unable to approximate perfectly the forefinger and thumb, hence he cannot pick up a pencil from the table nor button his clothes. Sensibility to heat and cold is natural. He can imperfectly localise impressions. He complains of pins and needles, and of numbness in both hands. The same sensations are felt in the legs, behind the knees. He complains of pain and tenderness on pressure over the lumbar region. On the application of the hot-sponge test nothing unusual is elicited. There are no ataxic symptoms.

Sight is dim, and has been failing for the past two years. The pupils are contracted. The fundus cannot be distinctly seen, owing to opacity of the vitreous.

The other special senses are normal.

The reflex functions (defecation, urination, swallowing, etc.) are normal.

Circulatory System.—The heart-sounds are very weak. There is a soft systolic apex murmur. The area of cardiac dulness is small. The radial pulse numbers 56, and is very soft and weak, slightly visible and jerking.

The *Respiratory* and *Urinary* systems are normal.

The appetite is good, tongue clean, bowels regular. The liver and spleen seem of normal size.

On Microscopical Examination of the Blood, it was found that the red corpuscles went into clusters, but did not form rouleaux. Many of them were tailed. Many of them were smaller than natural. The appearance of apparent nucleation was not seen. The white corpuscles were slightly in excess.

The *Treatment* consisted in the administration of iron, quinine, cod-liver oil, lime-juice, and arsenic, in the order named, together with a liberal diet.

The patient improved slowly at first, but after commencing the arsenic the improvement was marked and rapid. During his stay in hospital the urine once or twice contained a trace of albumen, but no casts.

He was discharged on 22nd July, saying he was fit for work. The duration of his stay in hospital was 126 days.

Remarks.—The diagnosis in this case was not so certain as in those previously related. The condition was one of profound and apparently causeless anæmia, with marked changes in the microscopical characters of the red blood globules. So far it resembled progressive pernicious anæmia. The increase in the white corpuscles, and the emaciation, and the dry wrinkled condition of the skin, were opposed, however, to this view of the case.[1] The intensity of the reflex movements was remarkable; indeed, so great was it, that a condition of incomplete pseudo-paraplegia was produced, the debilitated condition of the patient partially contributing thereto. The intensity of reflex movement and the diminution of sensibility were no doubt due to the malnutrition of the nerve-centres.

Case V. Profound Anæmia following Pregnancy. Vomiting. Diarrhœa. Retinal Hæmorrhages. Death. No Autopsy.

Mary B., æt. 29, a married woman, living at North Shields, was seen by me in consultation with my brother, Dr. J. W. Bramwell, on 14th September 1875.

Previous History.—She was quite well until after her last confinement, which took place eight months ago. Since that date she has been gradually getting paler and weaker. She knows no cause for her illness. The labour was easy, and not followed by any excessive discharge. Of late she had suffered from vomiting and diarrhœa. She has not menstruated since her confinement. She weaned her child some months ago.

Present Condition.—She was profoundly anæmic, but remarkably well nourished. The face was slightly swollen, and of a greenish-yellow hue. The skin was very smooth and ivory-like. The pupils were equal, and moderately dilated. The sight had been dim for three months. There were well-marked hæmorrhages in both retinæ; the discs were very pale, the vessels almost empty. She complained of pains and giddiness in the head. She was unable to sit up; when she attempted to do so, she felt giddy and faint. Loud blowing murmurs were heard at the base of the heart, and in the vessels of the neck. The heart seemed slightly increased in size. Before she took to bed she frequently suffered from palpitation. The urine was copious in amount, very pale, sp. g. 1010. It was free from any deposit, and contained no albumen. A drop of blood was placed on a slide, and was examined half an hour afterwards. Unfortunately, owing to the delay and the changes which had taken place during the transit, the examination could not be relied upon.

The abdomen was natural; the liver and spleen were both slightly increased in size.

Subsequent Progress of the Case.—There were two or three attacks of diarrhœa after my visit, and the patient gradually sank. She died towards the end of September.

Notwithstanding every effort, a post-mortem could not be obtained.

Case VI. Profound Anæmia. Retinal Hæmorrhages. Marked Alteration in the Red Blood Corpuscles. Palpitation. Dyspnœa. Hæmic Murmurs. Vomiting. Diarrhœa. Œdema of face, feet, and hands. No Emaciation. Recovery under Arsenic.

John D., æt. 38, married, a chemical worker, was admitted on 26th November 1875, complaining of shortness of breath and

[1] For further remarks on the diagnosis of Progressive Pernicious Anæmia, see my Clinical Lecture in the *Medical Times and Gazette* of 20th October 1877.

palpitation on the least exertion, swelling of the face, hands, and feet, and general debility.

Previous History.—He was a healthy man until seven months ago, when his present illness commenced. It was brought on, he thinks, by exposure to cold and wet. He took a shivering. This was followed by general weakness. His colour has undergone a marked change, and his hair has become greyer than it used to be. He has several times vomited, and has had frequent attacks of diarrhœa. Three months ago he was jaundiced; two months ago his face swelled; two weeks ago his feet became œdematous. He lives in a fairly healthy house, and has had abundance of good and varied food. He thinks 'the gas' was partly the cause of his complaint. Has been a fairly steady man. Has not had syphilis.

Family History.—Good.

Present Condition.—He looks sixty years of age. The feet, face, and hands are slightly swollen. He is extremely anæmic. The skin has a yellow tinge. The hair is grey. The conjunctivæ are pale. There is a small deposit of fat at each internal canthus. There is no emaciation, but the muscles are soft and flabby. Muscular irritability is marked. His weight is 11 st. 11 lbs.

The *Temperature* is normal.

He is short of breath, and suffers from violent palpitation on the least exertion. He often, too, feels giddy and faint. Loud blowing murmurs are heard at all the cardiac orifices. A mitral murmur, systolic in time and propagated upwards towards the left axilla, being specially noticeable. Indeed, so marked was it, that Dr. Mickle, the junior house-surgeon, diagnosed the case as one of cardiac dropsy from mitral insufficiency. The size of the heart is natural. The pulmonary second sound is not accentuated. The radial pulse is 76, regular, and of fair strength.

There is a loud venous hum in both sides of the neck. The left external jugular vein is distended and prominent.

On microscopical examination, the Blood was found to present exactly the same character as in the case already described.

The tongue is clean and moist, but pale; the appetite good; there is no thirst. He vomits occasionally, and is subject to frequent attacks of diarrhœa.

The *Liver* dulness measures 4½ inches. The splenic dulness seems slightly increased.

The *Thyroid* gland is not enlarged.

The *Respiratory System* is normal.

The *Urine* is very pale, neutral, sp. g. 1020. It is slightly darkened by heat and nitric acid, but contains no albumen.

He sleeps fairly well; occasionally suffers from headache. He complains of numbness in the hands and feet, especially after exposure to cold. Violent reflex movements are produced on tickling the soles of his feet. He feels unsteady when he walks. His gait is natural, and he stands steadily with his eyes shut. He complains of pain in the back, and of slight tenderness on pressure over the lumbar region. The application of the hot-sponge test shows nothing abnormal.

Sight is dim in both eyes. The pupils are dilated, but very sensible to light. The fundus is very bloodless, the disc somewhat ill-defined. There are no retinal hæmorrhages.

He complains of a singing noise in the left ear. The other special senses are normal.

Treatment.—He was ordered five grains of sulphate of quinine, and fifteen drops of the tincture of the muriate of iron three times daily.

Subsequent Progress of the Case.—*On 3rd December* he was ordered a teaspoonful of phosphorised cod-liver oil three times daily ($\frac{1}{60}$ gr. of phosphorus).

On 6th December the eyes were again examined with the ophthalmoscope, and several large retinal hæmorrhages were seen. The hæmorrhages were evidently recent; the stratum of blood seemed very thin. (It is interesting to note the fact that a few drops of atropia had been placed in each eye, and that extreme dilatation had resulted therefrom. It was only after this dilatation had continued for some days that the retinal hæmorrhages were observed.)

15th December.—He was much worse. The temperature yesterday was 100·2° F., the pulse 120. The iron was discontinued, and liq. arsenicalis substituted, two drops thrice daily.

18th December.—Dose of liq. arsenicalis increased to iv. minims.

28th December.—Dose increased to vi. minims.

31st December.—Feels better. The numbness is less. There is more œdema than on admission. The liver dulness measures 6 inches. The splenic dulness is also increased.

11th January.—Very much better. Shortness of breath less. Colour more natural. The dose of liq. arsenicalis increased to viii. minims.

20th January.—So much better that he asked to be made an out-patient. The dose of liq. arsenicalis increased to xii. minims.

6th March.—Still improving. Dose of liq. arsenicalis increased to xvi. minims.

24th April.—Says he never felt better in his life. His colour is now quite natural. His hair is in places growing darker. He is not in the least short of breath. All cardiac murmurs have disappeared. He looks fifteen years younger than he did when admitted to hospital. The blood is now normal. Sight is still a little dim.

Remarks.—This case is of great interest, from the fact that recovery took place, and was clearly due to the administration of arsenic. The same good effects also followed the use of the drug in Cases I. and IV., already related.

In Cases I. and IV. the drug was used empirically, for I was not then acquainted with the post-mortem appearances, one of the most important of which is fatty degeneration of the heart. Now it is well-known that arsenic is a most valuable cardiac tonic, and that it is especially useful in cases of fatty degeneration. Remembering this, and also the fact insisted upon by the late Dr. Anstie, that arsenic is a most valuable blood tonic, I gave it, and pushed it in Dunn's case.

Although the result was all that could be wished for, I would not for a moment have it supposed that arsenic will be found a specific for the disease. It is impossible to reason on a single case, however successful. This remedy has been tried without any good result by Dr. Samuel Fenwick[1] and others.

The explanation of his failure probably is that we have not to deal with a single diseased condition, but that idiopathic anæmia, just like anæmia in general, is the product of various morbid processes, and represents the very last stage of the anæmic process (*Professor Quincke's Clinical Lecture, Medical Times and Gazette*, 14th October 1876).

It is, however, highly satisfactory to be able to point to a single case in which recovery so obviously followed treatment, and that in a disease which in the experience of many is uniformly fatal.

Subsequent History of the Case.—Professor Philipson has kindly sent me the following notes which show the subsequent history of the case:—

The patient was readmitted to the Royal Infirmary, Newcastle-on-Tyne, on 8th November 1888, suffering from general weakness and profound anæmia of nine months' duration.

He stated that after his discharge from the Infirmary in April 1876 he had a relapse and was laid up for twenty-two weeks. He recovered under the same treatment (arsenic) which had been previously adopted, and has remained well until the present relapse occurred nine months ago.

Condition on Admission (November 8, 1878).—The patient has a sallow cachectic appearance. His weight now is 10 st. 9 lbs.; nine months ago he weighed 11 st. 5 lbs. An arcus senilis is present in both eyes. The lips are anæmic, the teeth much decayed. There are no hæmorrhages in the retina. A systolic murmur is present in the mitral area. The knee-jerks are entirely absent. There is slight ankle clonus in the right leg. Sensation distinctly delayed. No ataxia.

3rd December.—Red corpuscles number 1,200,000 per cubic millimetre; many of them are altered in size and shape.

The patient was placed on arsenic (Fowler's solution), which was gradually increased from 5 minims on 16th November to 14 minims on 13th January.

Result.—Under this treatment steady improvement occurred. The patient was discharged very greatly improved on 19th January. The red blood corpuscles then numbered 1,700,000 per cubic millimetre, and the hæmoglobin equalled 52%.

After his discharge the patient remained well until August 1889. The anæmic symptoms again returned, together with diarrhœa and extreme weakness and prostration. The patient died at the end of August 1889.

NOTE.—It will be observed that this patient remained quite well for twelve years; a relapse then took place; marked improvement again occurred under arsenical treatment; finally death occurred in August 1889 as the result of diarrhœa and a return of the anæmic symptoms.

[1] *Lancet*, 21st July 1877, page 78.

THE CLINICAL INVESTIGATION OF CASES OF PERNICIOUS ANÆMIA.

In studying cases of pernicious anæmia during life, the following points in particular should be noted :—

Preliminary Facts.—Name. Age. Sex. Married or single (if married, number of children or miscarriages). Occupation. Station in life. Circumstances and surroundings (whether well fed, well clothed, well housed, well cared for, accustomed to heavy or laborious work, exposed to strain, injury, etc.). Place of residence. Place of birth. Date of examination. Complaints.

Family History.—Whether any of the patient's near relatives have been affected with pernicious or any other form of profound anæmia. Whether the patient inherits a tendency to any special form of disease (gout, etc.).

Personal History and Etiology.—The condition of the patient's health prior to the date at which the first symptoms of the disease (pernicious anæmia) were developed. The nature and date of any previous illnesses (malaria, yellow fever, etc.). Whether the disease was slowly and gradually or rapidly developed. Whether there was any apparent cause for the development of the disease, such as dyspeptic troubles, diarrhœa, mental anxiety, strain, prolonged loss of blood, malarial poisoning, yellow fever, prolonged lactation, pregnancy, intestinal parasites, etc.

The mode of onset and the mode of development of the symptoms.—The exact date at which the symptoms were first noticed. The nature of the first symptoms (pallor, shortness of breath, etc.).

Present Condition and Symptomatology.

1. *Symptoms of which the patient complains.*—(Debility, shortness of breath, palpitation, giddiness, tinnitus aurium, swelling of the feet, etc.).

2. *Colour of the skin and mucous membranes.*—(Pallor, lemon yellow tint, jaundice, etc.).

3. *General state of nutrition.*—(Well or ill nourished; whether the body fat is preserved; whether the muscles are soft and wasted; whether the skin is soft and smooth or dry and harsh; etc.).

4. *The condition of the blood.*—(a) Appearance of a drop of blood obtained by puncturing the unbandaged finger. (b) The number of the red blood corpuscles. (c) The total percentage of hæmoglobin. (d) The individual richness of the red blood corpuscles in hæmoglobin. (e) The number of the white corpuscles. (f) The microscopical character of the red blood corpuscles—whether they form rouleaux, their colour, size—megalocytes, microcytes—their shape—poikilocytosis—concentration of hæmoglobin in localised areas of, vacuolation of, nucleated red corpuscles, deeply stained red corpuscles of small size (Eichhorst's corpuscles). The white corpuscles (size, appearance, etc.). Max Schultze's granular masses. Blood platelettes. Organisms, etc.

5. *Hæmorrhages.*—The presence or absence of retinal hæmorrhages, petechiæ, epistaxis, bleeding from the gums and throat, hæmatemesis, bleeding piles, etc., should be noted.

In examining the retina with the ophthalmoscope, the condition of the optic discs (colour, presence or absence of œdema, papillitis, etc.) should be noted.

6. *The temperature.*—This should be carefully noted throughout the course of the disease, since febrile attacks are of frequent occurrence.

7. *The condition of the urine,* especially whether dark-coloured, whether it contains pathological urobilin, microscopical granules of pigment, excess of uric acid, etc.

8. *The condition of the circulatory system.*—Whether the action of the heart is unduly irritable; the position of the apex beat; the nature of the cardiac impulse (diffused, flickering, etc.); the size of the heart as determined by percussion, the presence or absence of cardiac murmurs in the mitral, pulmonary, tricuspid and aortic areas, their rhythm, sound, characters, etc.

The exact condition of the pulse (frequency, fulness, regularity, etc.).

The presence of a venous hum in the neck, etc.; the presence of distended veins or of true pulsation in the veins of the neck, etc.

9. *The condition of the digestive system.*—Anorexia, thirst, nausea, vomiting, diarrhœa (the character and frequency of the motions, and especially the presence or absence of ova or intestinal parasites in the stools). The condition of the tongue (pale, smooth, furred, dry, etc.). The presence or absence of bleeding piles, etc. The condition of the liver and spleen.

10. *The condition of the nervous system.*—Giddiness on effort, irritability of temper, loss of memory, tinnitus aurium, uneasiness and restlessness, drowsiness, epileptiform convulsions, coma, etc.

11. *The condition of the respiratory system.*

12. *The condition of the generative organs.*—Menstruation, uterus, ovaries, etc.

Treatment.—The treatment adopted and its results.

The subsequent progress of the case.—The red blood corpuscles should be counted, the hæmoglobin estimated and the microscopical characters of the blood noted at least once every week.

Intercurrent complications.

Duration.

Result.

Post-mortem appearances.—In examining cases of pernicious anæmia after death, every organ and part should be exhaustively examined and attention specially directed to the following points :—

1. The colour of the skin, subcutaneous fat, muscles, etc.

2. The presence of petechial hæmorrhages in the skin, pleura, pericardium, brain, retina, etc.

3. The exact position of the tip of the appendix of the left auricle, whether it overlaps the pulmonary artery, whether it is seen from the front when the pulmonary artery is exposed, etc.

4. The condition of the heart (size, shape, weight, whether the muscular tissue is fatty, the condition of the valves, etc.).

5. The condition of the stomach (size, the naked eye and microscopic condition of the mucous and other coats).

6. The condition of the intestines (presence of ulceration, intestinal worms, etc.).

7. The condition of the spleen (size, weight, naked eye and microscopic characters, especially whether these organs contain an excess of iron or not).

8. The condition of the liver (size, weight, naked eye and microscopic characters, especially whether the organ contains an excess of iron or not).

9. The condition of the kidneys (size, weight, naked eye and microscopic characters, especially whether the kidneys contain an excess of iron or not).

10. The condition of the brain, retina (colour, hæmorrhages, etc.).

11. The condition of the bone-marrow (naked eye and microscopic).

ALOPECIA AREATA

Synonyms.—Area; Alopecia circumscripta; Alopecia declavans

In this comparatively common disease, which is represented in Plate XCV., bald patches are developed here and there over the scalp, and it may be, though this is comparatively speaking rare, on other hairy parts of the body. The rare form alopecia universalis is represented in Plate XCVI.

Etiology.—In many cases the loss of hair is rapidly produced. The affected areas may become completely bald in the course of two or three days.

In some cases the loss of hair has been preceded by a mental shock or profound constitutional disturbance; in a few cases by neuralgic pains in the area of the scalp which subsequently becomes bald.

The disease appears to be slightly more common in men than in women; and in dark-haired than in light-haired people.

The disease usually develops in youth and early adult life, rarely after the age of 40, almost never in old age.

In some families there is perhaps a special liability to the disease, for cases are sometimes met with in which more than one member of a family is affected, an interval of some years separating the individual attacks.

The exact cause of the condition is unknown. Two theories—the neurotic and the parasitic—have been advanced to account for the disease; and it is probable that both are correct; in other words, it is probable that more than one condition may give rise to very similar appearances (bald patches exactly resembling those of alopecia areata); but it does not seem to be always possible to differentiate the two forms—the neurotic and the parasitic—by our present means of investigation.

In favour of the neurotic view are the facts:—That in some cases the development of the disease is preceded by nervous shock; the sudden development of the bald patches; that in rare cases the bald patches correspond in distribution to the areas of distribution of particular nerves; that in some cases the development of the bald patches is preceded by neuralgic pains in the parts of the scalp which subsequently become affected; that in rare cases the innervation of the scalp over the bald areas is disturbed (anæsthetic or hyperæsthetic); and that many authorities doubt whether the micro-organisms which have been found by some observers in the affected areas of the scalp are actually the cause of the disease.

The chief facts in favour of the parasitic theory are:—That micrococci have been detected in the lymph spaces and hair follicles by A. K. Robinson,[1] Vaillard and Vincent,[2] Sabouraud[3] and other observers, and that in some cases the disease appears to be contagious.

[1] *Monateshefte für Praktische Dermatologi*, 1888, January and December.
[2] *Annales de l'Institut Pasteur*, vol. iv., 1890, p. 446.
[3] *Annales de Dermatologie et de Syphiligraphie*, T. vii., 1896. For a detailed review by Dr. Leslie Roberts of this imporant research, see the *British Journal of Dermatology*, November 1896, p. 451.

Sabouraud, as the result of a long series of most careful observations, claims that in the early stages of the disease a micro-bacillus is always present in enormous quantities in dilated portions of the hair follicles, but it remains to be proved whether these organisms are actually the cause of the disease. The micro-organisms disappear in the later stages of long-continued cases. Numerous cases have been described, more especially by French writers, in which the disease appears to have been propagated by contagion; but this is certainly exceptional. And in this connection it must be remembered that there is a close similarity between alopecia areata and the rare form of ringworm termed bald ringworm. In short, it is highly probable that in some of the cases in which alopecia areata was supposed to be propagated by contagion the disease was ringworm. Liveing and others have recorded cases of so-called bald ringworm in which the affected areas of the scalp were quite bare from the first and exactly resembled the patches of alopecia areata except as regards their shape, some of them being angular rather than round or oval. Liveing states that some of these cases of rapidly produced bald ringworm could only be definitely distinguished from alopecia areata by the fact that at the margins of the bald area (over which there were no stubbly or broken down hairs) some of the hairs were diseased and on examination showed distinct fungus elements.[1] Further, Mr. Jonathan Hutchinson states that in many of the cases of alopecia areata which have come under his notice the patients had previously suffered from ringworm, or had been in contact with children affected with ringworm. This is certainly contrary to my own experience. In the comparatively small number of cases of alopecia areata which have come under my own notice, careful enquiry has almost invariably failed to elicit a history of ringworm either in the patient or in other members of the patient's family.

Crocker thinks that under the generic term 'alopecia areata' there are at least four classes of cases which should be separated from each other.

In the *first* group he places those cases in which the alopecia is universal, and in which the hair does not necessarily come out in patches, but in which there is general falling off, often very rapid, and accompanied in some cases by changes in, or even falling off of, some or all of the nails. These cases are very rare.

In the *second* group, cases which are also very rare, one or more bald patches develop at the site of an injury or in the course of a recognisable nerve.

In the *third* group, he places the forms originally described by Neumann as alopecia circumscripta seu orbicularis. In

[1] Quain's *Dictionary of Medicine*, vol. i. p. 52.

this form the patches are circular and always small—from a lentil to a pea in diameter—much depressed below the surface, with often a marked decrease of the sensibility. It is in his experience a rare form and the prognosis is very unfavourable.

'Few,' he says, 'would dispute that all three of these classes are essentially of a tropho-neurotic character. Taken collectively they form a very small proportion of cases classed as alopecia areata—certainly not 10 per cent., and I believe not more than 5 per cent.'

The *fourth* group comprises the great majority (90 or 95 per cent.) of cases of alopecia areata and represents the ordinary common form of the disease.

Crocker believes that in these cases a fungus can be demonstrated in recent cases if rightly looked for. 'It is no use looking on the bald places themselves, it is no use looking in atrophied (!) hairs; the fungus is never in the shaft, but on it or the attached epithelium. The best way is to pull out a good many of the loose hairs at the border of the bald area, then to examine these with a lens, and select those hairs which have most root-sheath attached, rejecting those with smooth atrophied roots, and then, taking the selected hairs, cut off the greater part of the superfluous shaft, soak these root ends in liquor potassæ or a saturated solution of caustic potash in glycerine, and examine the portions of epidermis attached to the shaft; it should not be manipulated too much, or the affected part may get detached from the shaft and be lost. The fungus is always in small foci, and perhaps only in one of several selected hairs; sometimes it may be seen at the very extremity of the root, as if it had worked round and separated the hair from its papilla.'

He sums up his conclusions with regard to these cases as follows:—'With regard to the fourth class the preceding facts show:—1. That this form is to a limited extent contagious, and that from time to time limited outbreaks have occurred in small communities. 2. That not only children, but adults who have been in contact with tinea tonsurans sometimes develop bald patches indistinguishable from alopecia areata. 3. That in tinea tonsurans commencing in the typical way the typical crooked stumps may both spontaneously and under treatment disappear, and the patches develop into an alopecia areata condition with (!) hairs. 4. That in those countries where tinea tonsurans is most common alopecia areata is also most frequent. 5. Hence we must conclude that a large proportion of cases in adults which are termed alopecia areata are cases of bald tinea tonsurans which is acknowledged to exist amongst children, and that the old authors, from Bateman onwards, were justified in calling it porrigo or tinea declavans. 6. Finally, I believe that a parasite indistinguishable from the trichophyton tonsurans fungus may be demonstrated in recent cases, and the treatment most efficacious is inunction of powerful and stimulating parasiticides.'[1]

Clinical History.—One of the most remarkable features of the disease is the rapidity with which the patches are produced. Malcolm Morris states that he has 'seen the entire hair of the body shed within forty-eight hours.'[2]

The parts of the scalp which are most frequently affected are:—the occipital region, over the ridge of bone into which the trapezius muscle is inserted; behind or above the ear; and on one or other side of the vertex; but any part of the scalp may be affected. In rare cases the bald patch corresponds to the area of distribution of a particular nerve.

In the ordinary form of alopecia areata, i.e. cases in which the loss of hair is confined to individual portions of the scalp, the bald patches are rarely symmetrical except in the occipital region and on the vertex. The number of the patches varies in different cases. The shape of the patches is usually round or oval, in some cases oblong, or, if they run together, somewhat triangular. Their size varies considerably in different cases. In some cases, the individual patches run together forming large bald areas. In other cases, the whole scalp becomes absolutely bald. In rare cases, every part of the body is destitute of hair. To this condition, which is admirably represented in Plate XCVI., the term *alopecia areata universalis* has been applied.

In typical cases the appearance of the patch is highly characteristic. The margins are usually sharply defined. The affected area of the scalp is usually quite bald and has a smooth, shiny, polished appearance. (See Plate XCV.) Isolated hairs or tufts of hair in some cases remain in the midst of the otherwise bald area. There is no scaliness as in ringworm, but in exceptional cases a few broken and stubbly hairs may be detected at the margins of the bald area.

The affected area of the scalp is usually quite white (pale); in some cases in the early stages of the disease it is said to have a pinkish or reddish hue.

The hairs at the edges of the patch may be less firmly implanted in the scalp than normal. Crocker states that in all recent and active cases there are short hairs about one-eighth of an inch long, thickened at the free end, thin at the tapering point of insertion, so that these stumps look like an exclamation point (!). They pull out easily. The alteration appears to be due to an atrophy of the hair at its root.

Though these short atrophied hairs appear to be a constant feature in the early stages of alopecia areata, they are not absolutely distinctive of that disease; for in a case of bald ringworm described by Dr. Alder Smith[1] numerous short atrophied hairs having the exclamation-point shape were present.

In cases which have lasted some time and in which restoration of the hair is taking place, the bald patch is covered by fine, downy, unpigmented hairs.

In the great majority of cases the sensibility of the skin over the bald patch is quite unaffected; but in more than one recent case in which I have carefully investigated this point, I have found distinct evidence of nerve derangement—anæsthesia or hyperæsthesia.

In severe cases the portion of the scalp corresponding to the bald patch appears to be atrophied—thinner than normal or more tightly stretched over the bone. In some cases, the affected area of skull corresponding to the smaller patches is said to be slightly depressed below the level of the surrounding scalp.

The general health is usually good. Some of the patients are anæmic or neurotic; whether this is merely an accidental association or has a distinct etiological bearing on the disease is doubtful.

[1] *Lancet*, vol. i., 1891, pages 478 and 534.
[2] *Diseases of the Skin*, p. 472.

[1] *The British Journal of Dermatology*, 1895, p. 111.

Diagnosis.—The diagnosis of alopecia areata rarely presents any difficulty.

The mode of development (rapid loss of hair over localised areas of the scalp), the parts of the scalp which are affected (occipital region over the point of insertion of the trapezius muscle, behind and above the ear, and on one or both sides of the crown), the non-symmetrical arrangement of the bald patches, and the appearances of the bald areas (smooth, polished, and usually quite destitute of hair), are highly characteristic.

The differential diagnosis of alopecia areata and of ringworm.—In ordinary, typical ringworm the affected areas of the scalp are more or less rough and scaly, studded with broken, stubbly and diseased hairs; on being treated with chloroform (Duckworth's test) the affected hairs become white, and on microscopic examination the characteristic fungus can be demonstrated.

The close similarity which cases of 'bald ringworm' present to cases of alopecia areata has already been pointed out.

Dubreuille and Freche state[1] that in most cases of bald ringworm the change from the ordinary ringworm appearance to that suggestive of alopecia areata is usually partial and gradual, so that scurfy patches with broken hairs and bald patches can be seen together on the same scalp. In these cases the diagnosis is of course easy.

It is only when the baldness is rapidly produced, or when the case comes under observation after the appearances characteristic of ordinary ringworm (scurfy condition of the patches, and broken stubbly hairs) have completely disappeared that the diagnosis is difficult. In some cases of this kind, the only means of distinguishing the two conditions appear to be:—(a) the fact that the patient has been in contact with true ringworm; (b) the presence of diseased (broken, twisted, stubbly) hairs at the margin of the patch; and (c) the presence of characteristic ringworm spores and mycelium, on microscopic examination.

Prognosis.—This is usually favourable. Most cases get well in the course of time, but the condition may persist for months or even years.

In trying to form an opinion as to the curability and probable duration of any given individual case, the following are the chief points which have to be taken into account:—the duration of the disease, its extent and severity; the condition of the scalp (whether absolutely bald or covered with short downy hairs, whether atrophied or not); and the effects of treatment.

The longer the duration and the greater the extent of the disease, the worse the prognosis. An atrophied condition of the skin of the diseased area, and the persistence of the disease notwithstanding active treatment are also unfavourable indications.

The presence of fine downy hairs over the patch is always a hopeful indication.

In the rare cases of alopecia universalis the prognosis is most unfavourable. This condition is almost always, some authorities say always, incurable.

In the ordinary, localised, form of alopecia areata, relapses are not uncommon; the disease may develop again and again, the short or imperfectly formed hairs being shed more than once before a permanent cure takes place.

Treatment.—The indications for treatment are:—(1) to raise the tone of the general health to the highest possible state of efficiency: (2) to endeavour to promote the growth of the hair by stimulating applications; and (3), if, as some authorities believe, the disease is in some cases parasitic, to destroy the micro-organisms.

Amongst general and nervine tonics, arsenic, strychnine, phosphorus, cod-liver oil, and iron (if the patient is anæmic), are in my experience the most useful drugs.

In two of my cases I am satisfied that undoubted benefit resulted from the long-continued administration of small doses of thyroid extract.

Of local applications, acetum cantharidis, liquor episparticus, croton oil, veratria ointment (5 to 10 grains to the ounce), strong carbolic acid, corrosive sublimate and ammoniated mercury ointment are perhaps the most useful. The strength of the application should be sufficient to redden but not to blister the skin. Care must be taken not to apply the stimulating ointment or antiseptic lotion over a large area of the scalp at one time.

Electricity, both the faradic and galvanic currents, has also been recommended.

[1] *The British Journal of Dermatology*, 1896, p. 422.

DESCRIPTION OF PLATE XCV.

Figs. 1 and 2.—These figures represent a typical case of alopecia areata.

The patient, a boy aged 7, came under my notice as an outpatient at the Edinburgh Royal Infirmary on 30th June 1886. He had suffered from the disease for one year. The loss of hair had developed rapidly after a slight attack of scarlet fever. He was only seen once and I am unable to say whether the treatment which was recommended produced any benefit or not.

Figs. 3 and 4.—These figures represent a case of alopecia universalis.

The patient, a married woman aged 26, was seen at the Edinburgh Royal Infirmary on 18th February 1894. The condition had been present since she was six years of age. It had developed after an attack of measles. The loss of hair on the head was incomplete. Under prolonged treatment by thyroid extract, distinct improvement occurred, so far as the baldness of the scalp was concerned; but there was no growth of hair on the eyebrows and other parts of the body.

DESCRIPTION OF PLATE XCVI.

This Plate represents a typical example of universal alopecia which came under my notice a few years ago. The patient was a healthy young woman. The loss of hair had developed suddenly without any obvious cause, several years before I saw her. There was absolutely no hair on any part of the body. She had not suffered from ringworm. Various forms of treatment were employed, but without the slightest benefit.

DESCRIPTION OF PLATE XCVII.

This Plate, which represents a case of acute dementia, is copied by permission of the Council of the Royal College of Physicians, Edinburgh, from the original drawing in Sir Alexander Morrison's collection. The following description of the Plate is given :—

'Portrait of J. W., aged 25 ; a painter.

'The cause of this man's disorder was stated to be the intemperate use of strong liquors. It commenced with incoherence in his discourse and in his actions; he was soon after reduced to a state of apparent idiocy; fell down when placed on his feet; did not appear to comprehend the simplest question; his eyes were vacant; his regard was unsteady; he looked as if astonished. He was disposed to be obstinate and rather mischievous; he was, however, easily restrained. He had been four months in this state when his portrait was taken.'

DESCRIPTION OF PLATE XCVIII.

This Plate represents a patient suffering from chronic dementia. Formerly a patient in the Royal Asylum, Morningside, she was, when my artist Mr. Williamson painted her, an inmate of the Craiglockhart Poorhouse.

Dr. George M. Robertson has very kindly sent me the following commentary on the Plate :—

The absence of mind is expressed by :—(1) The general absence of tone—which, when present, denotes attention ; (2) the vacant or far-away appearance of the eyes—focussed for distance, the position requiring least expenditure of energy ; (3) the inaction of the corrugator supercillii ('the muscles of thought').

The patient is a bearded woman. The bearded condition in women is very much commoner in asylums than elsewhere. The explanation of this is as follows :—Every being inherits male characteristics from the father, and female characteristics from the mother; but only one group becomes potential, the other remains latent. In the case of a woman, the beard inherited from her father remains latent, owing to the potentiality of the mother's characteristics. When a woman reaches the climacteric, she loses her sexual characteristics to a great extent—she is less of a woman, and hence the male characteristics inherited from her father tend to become potential—there is a lesser force inhibiting them. Hence many women after the climacteric grow beards. This may occur also if disease attacks the ovaries. In the lower animals hens have been known to assume cock's feathers after they ceased laying. In dementia, sexual feelings—especially of the higher sort—soon tend to decay, and hence the greater tendency of the beard to grow.

DESCRIPTION OF PLATE XCIX.

This Plate represents a man aged 82, an inmate of the Craiglockhart Workhouse, affected with senile dementia. His sight and hearing were dull, he took little notice of his surroundings, spoke little, and seldom responded to questions. His appetite and general health were good.

DESCRIPTION OF PLATE C.

This Plate represents a case of lupus. The situation is quite typical. The nodulated character is well brought out in the drawing. The disease has not yet advanced to extensive ulceration. Around the margins of the affected area and on the chin, small outlying deposits ('satellites,' as Mr. Jonathan Hutchinson calls them) are seen. The patient was a woman who came under my notice in the Edinburgh Royal Infirmary some years ago.

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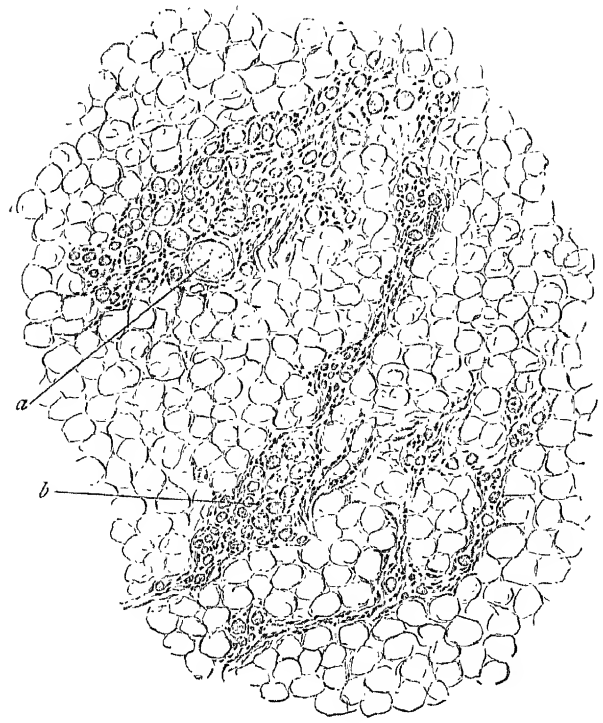


FIG. 4.—Pseudo-hypertrophic paralysis—transverse section of muscle. (Case IV., p. 98.)

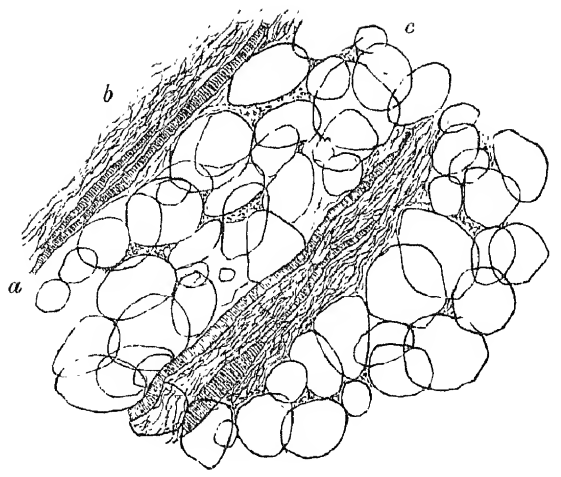


FIG. 5.—Pseudo-hypertrophic paralysis—longitudinal section of muscle.—(After Gowers.)

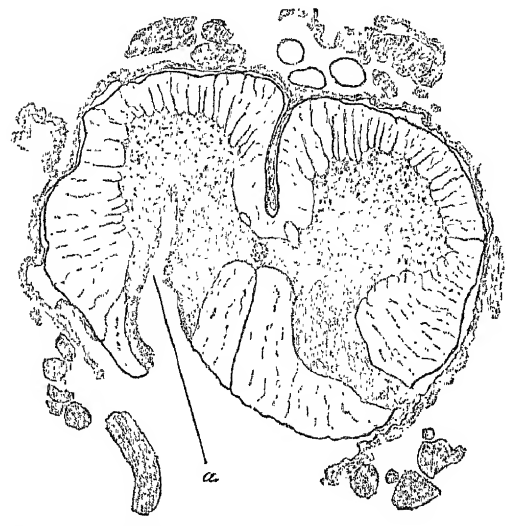


FIG. 2.—Spinal cord in pseudo-hypertrophic paralysis (?) Artificial lesion. (Case IV., p. 98.)

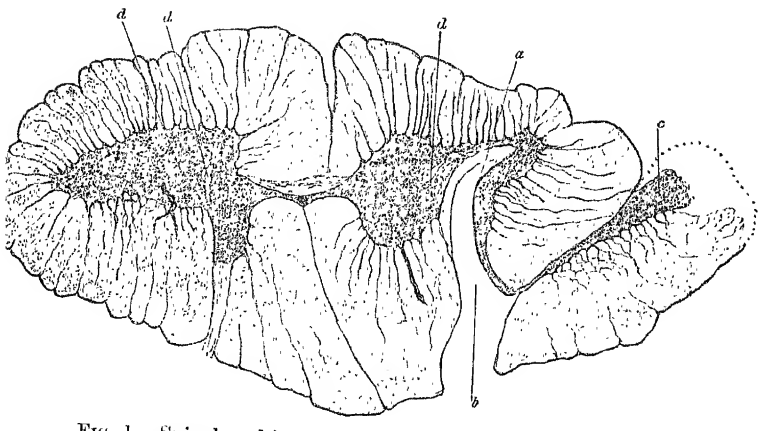


FIG. 1.—Spinal cord in case of pseudo-hypertrophic paralysis showing malformation of grey matter.

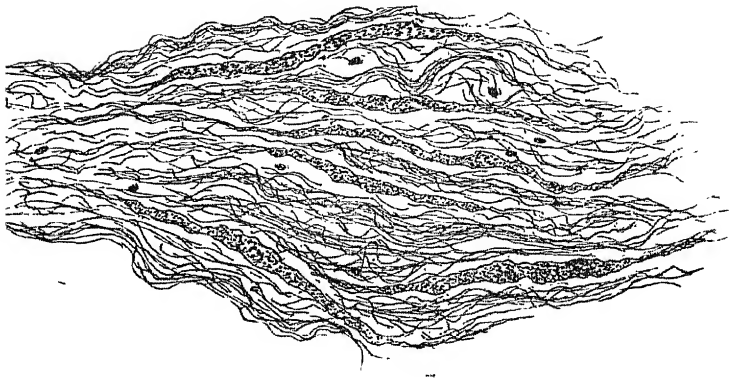


FIG. 6.—Heart muscle in pseudo-hypertrophic paralysis.

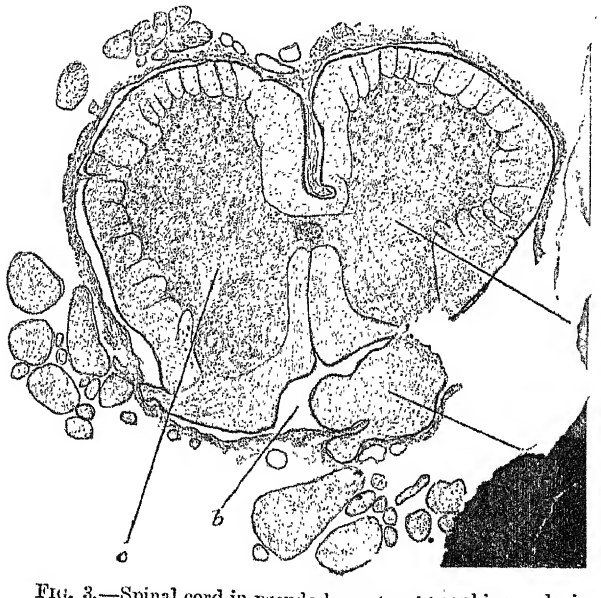


FIG. 3.—Spinal cord in pseudo-hypertrophic paralysis. (?) Artificial lesion. (Case IV., p. (p. 109.)

PSEUDO-HYPERTROPHIC PARALYSIS.

FIG. 1.

FIG. 2.

FIGS. 1 and 2.—Typical pseudo-hypertrophic paralysis. (Case I., p. 95.)

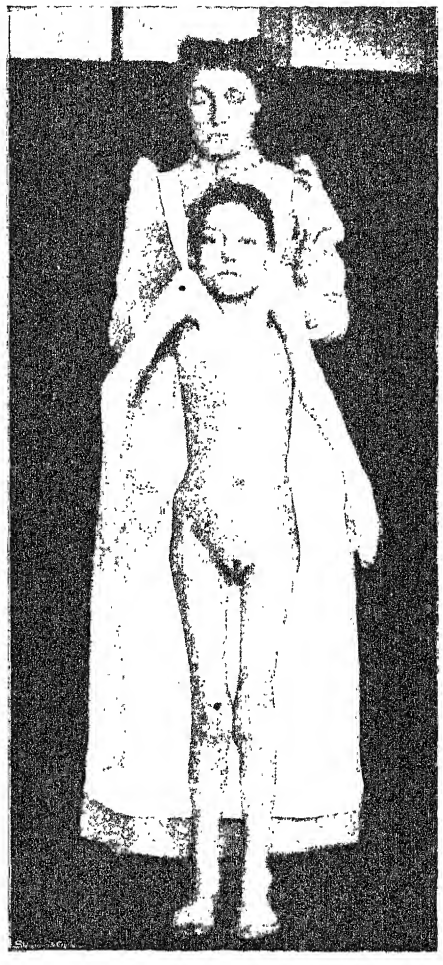


FIG. 3.—Atrophic form of progressive muscular dystrophy, showing non-fixation of shoulders. (Case XII., p. 107.)

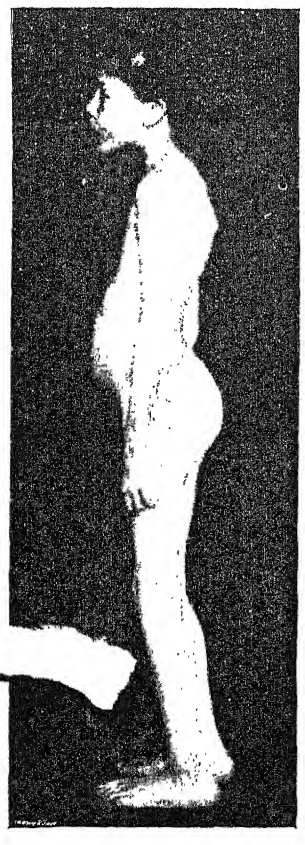


FIG. 4.—Atrophic form. (Case XII., p. 107.)

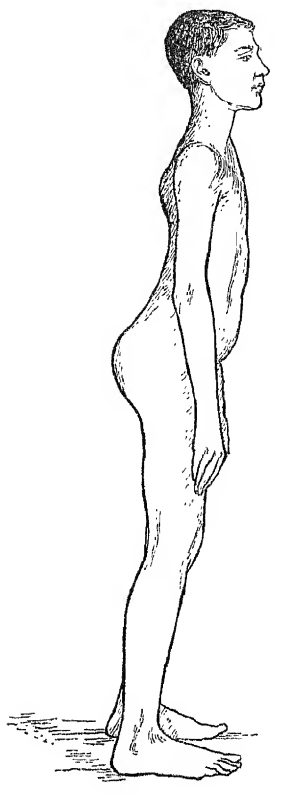


FIG. 5.—Pseudo-hypertrophic paralysis. (Case X., p. 104.)

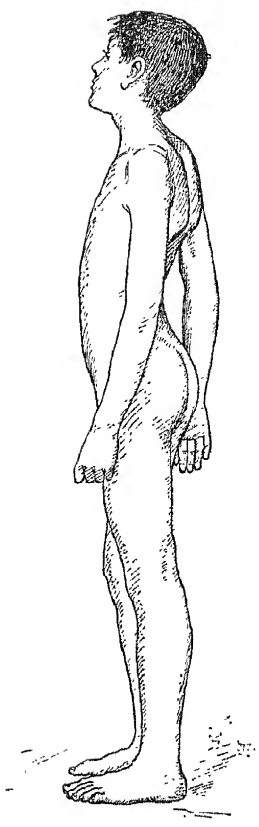


FIG. 6.—Leyden's form of progressive muscular atrophy. (Case IX., p. 103.)

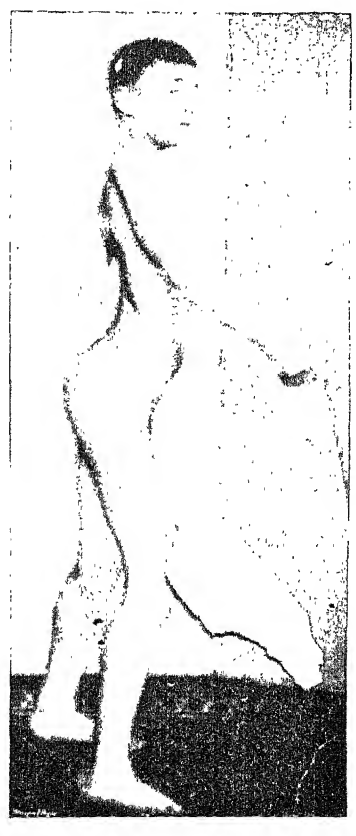


FIG. 7.—Pseudo-hypertrophic paralysis. (Case XV., p. 109.)

PSEUDO-HYPERTROPHIC PARALYSIS AND OTHER VARIETIES OF PROGRESSIVE MUSCULAR DYSTROPHY.

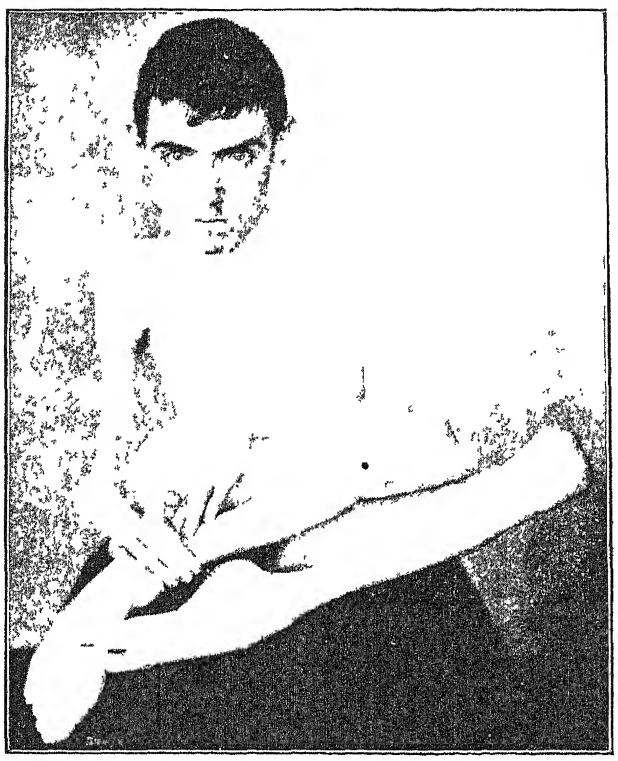


FIG. 1.

FIG 2

FIGS 1 and 2.—Advanced stage of pseudo hypertrophic paralysis (Case IV, p 98)

FIG 4 (Case VII, p 101)

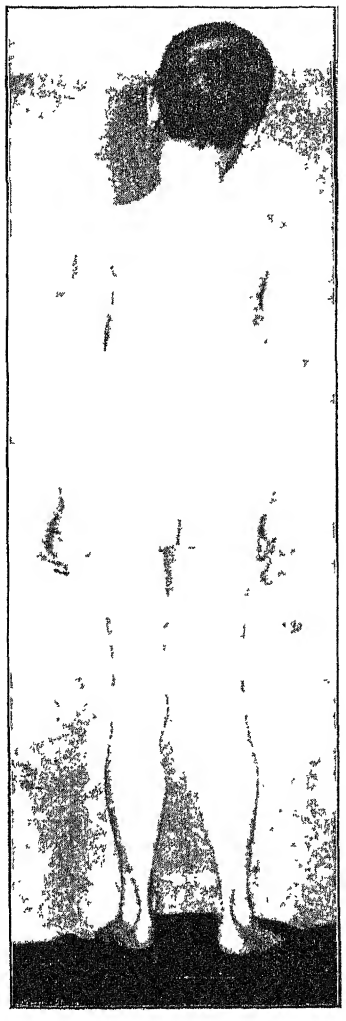


FIG. 3.—Pseudo hypertrophic paralysis—the brother of the patient represented in Figs 1 and 2. (Case V, p 100)

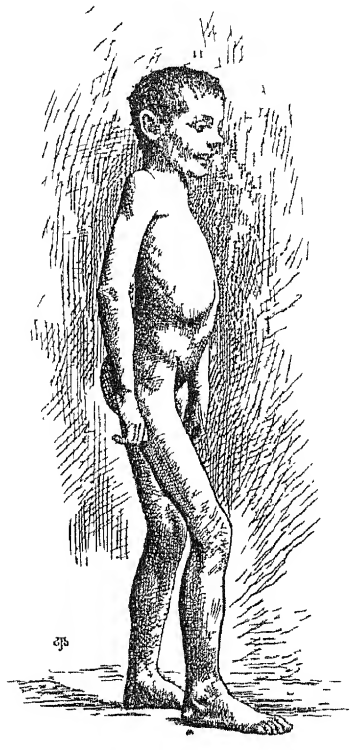


FIG 5 (Case VII, p 101)

PSEUDO-HYPERTROPHIC PARALYSIS.

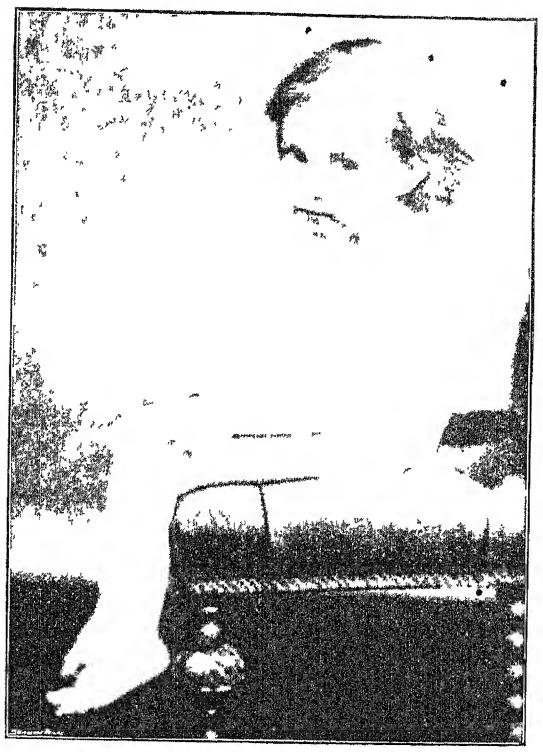


FIG 5

FIG 6

FIG 7

FIGS 5, 6 and 7.—Dr John Thomson's case of muscular atrophy in a child. (See p 92)

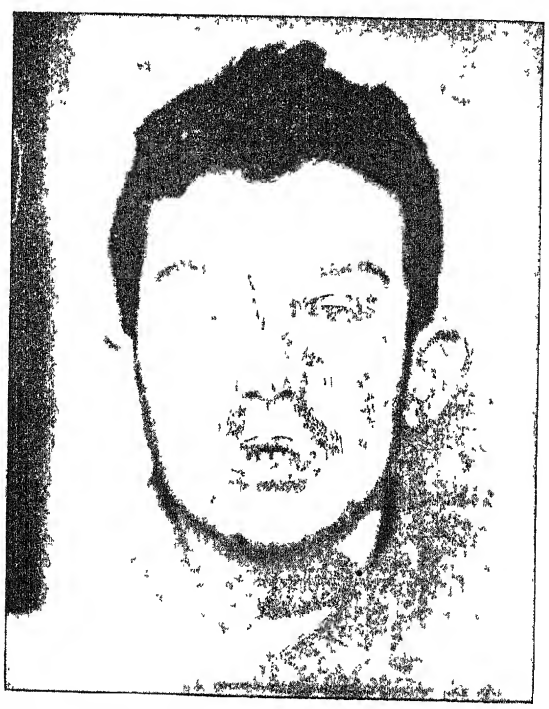


FIG 4.—Facio scapulo humeral type of progressive muscular dystrophy—attempting to whistle. (Case VIII, p 101)

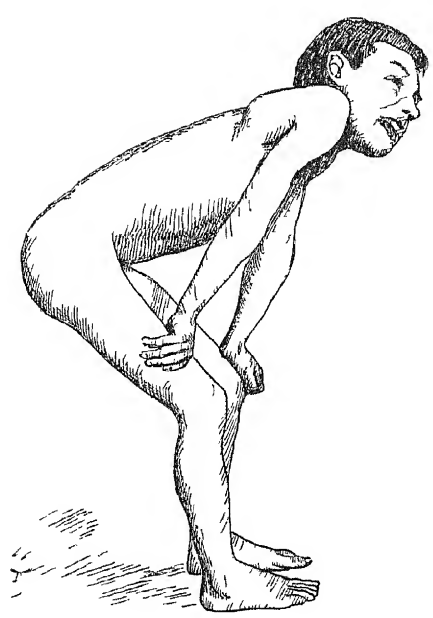


FIG 8.—Pseudo hypertrophic paralysis—the patient represented in Figs 1 and 2, Plate LXXVII. (Case I, p 95)

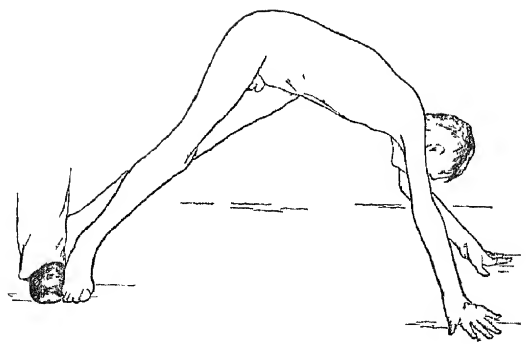


FIG 1.—Pseudo hypertrophic paralysis method of rising. (Case XI, p 106)

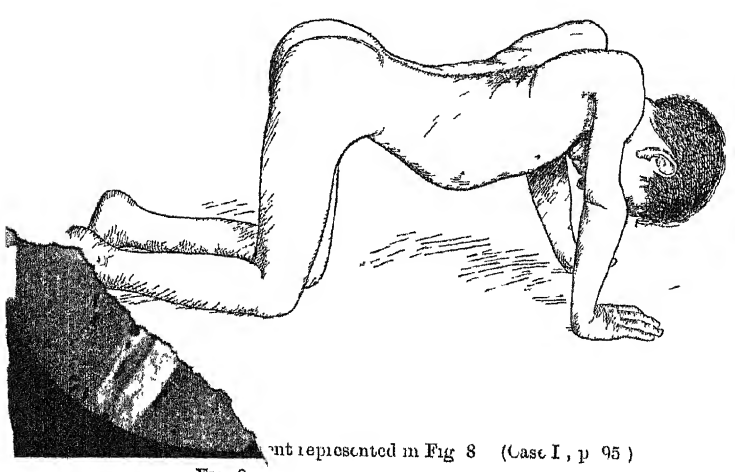


FIG 8

...ent represented in Fig 8. (Case I, p 95)

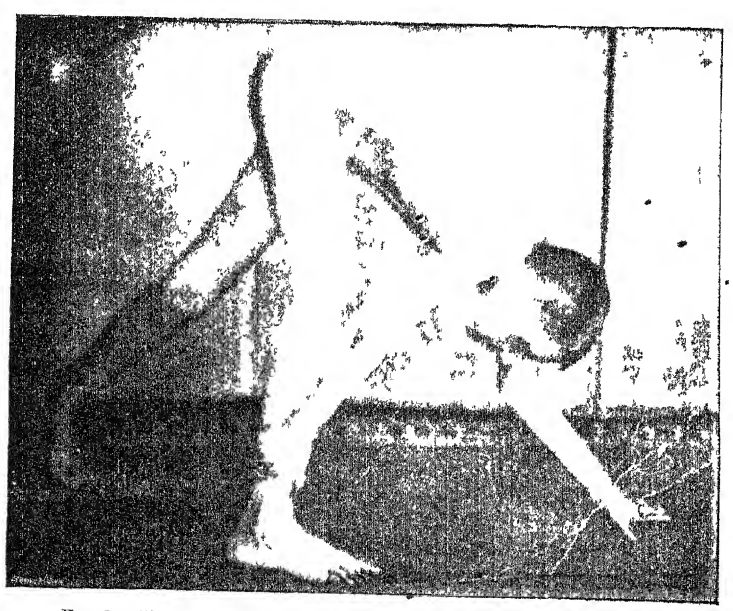


FIG 2.—The same patient represented in Fig 1. (Case XI, p 106)

MICROPHOTOGRAPHS OF MUSCLES IN PSEUDO-HYPERTROPHIC PARALYSIS AND MYOPATHIC ATROPHY

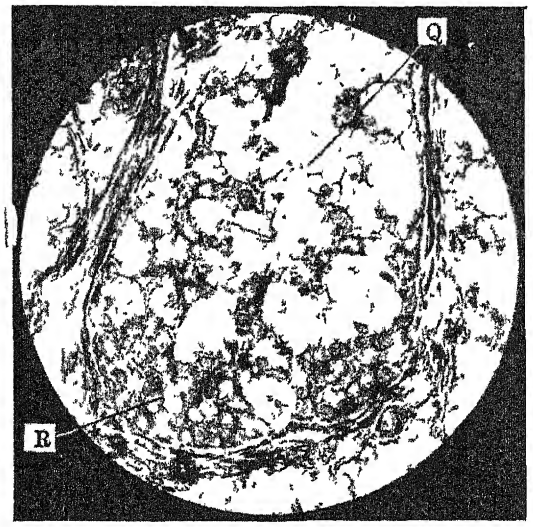


FIG. 1

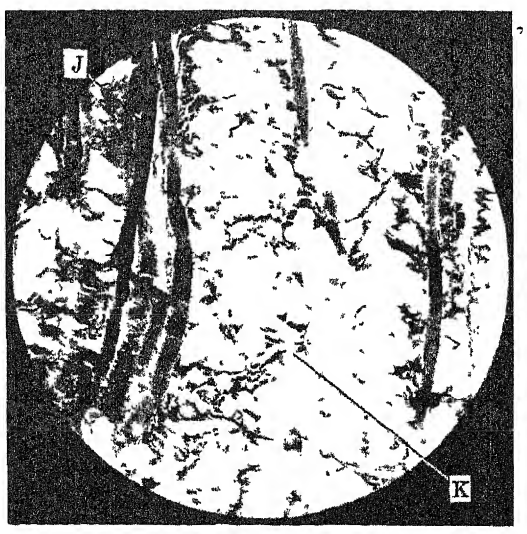


FIG. 2

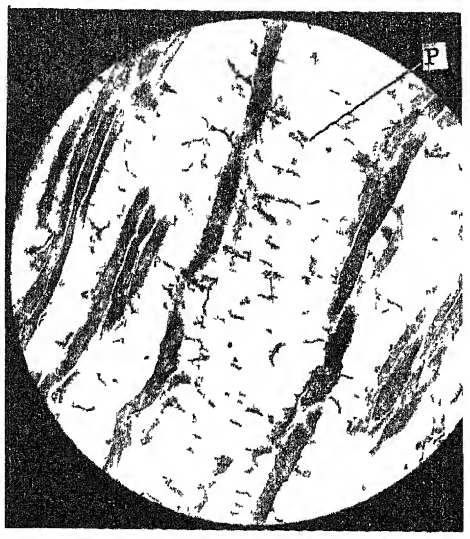


FIG. 12

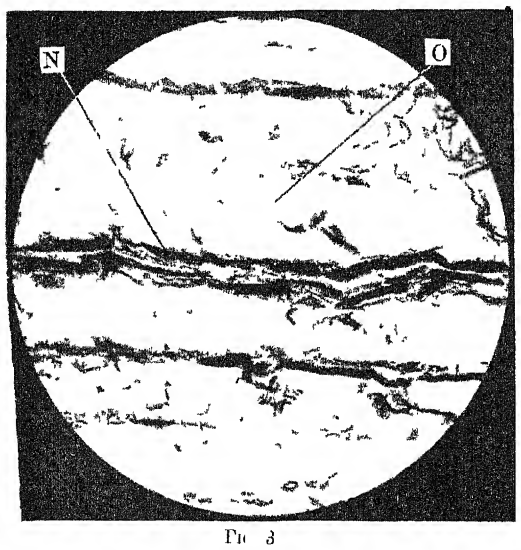


FIG. 3

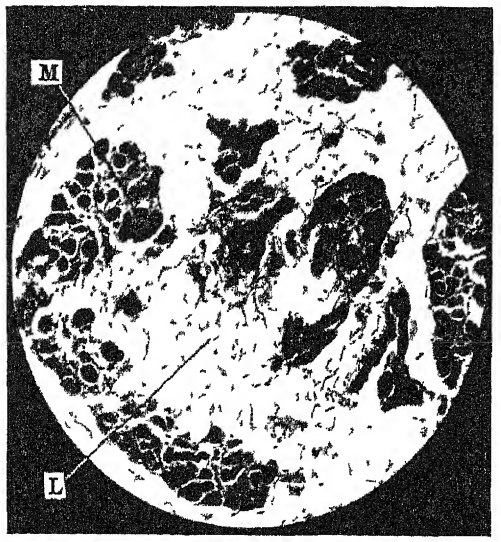


FIG. 4

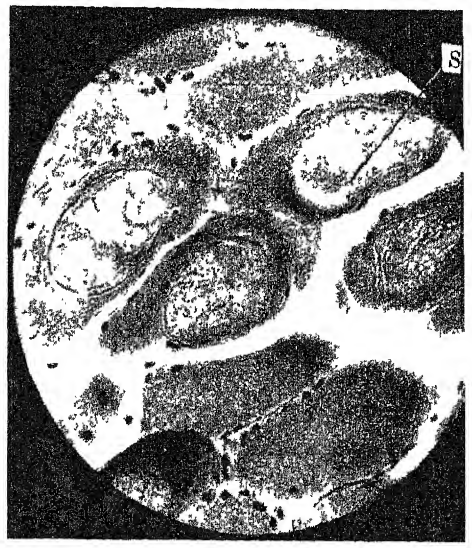


FIG. 11

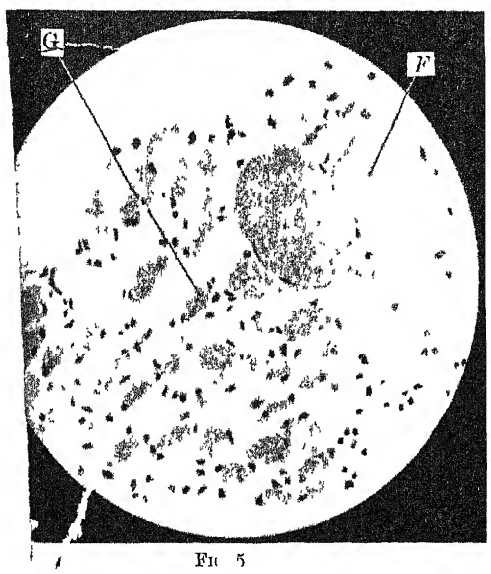


FIG. 5

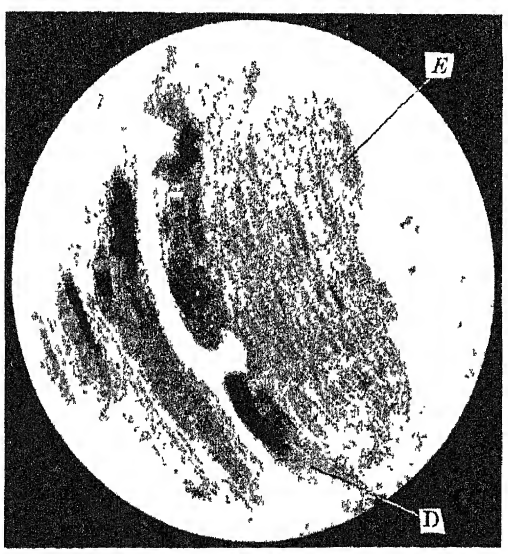


FIG. 6

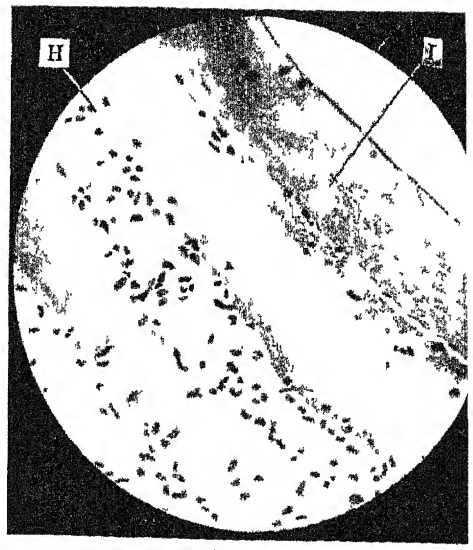
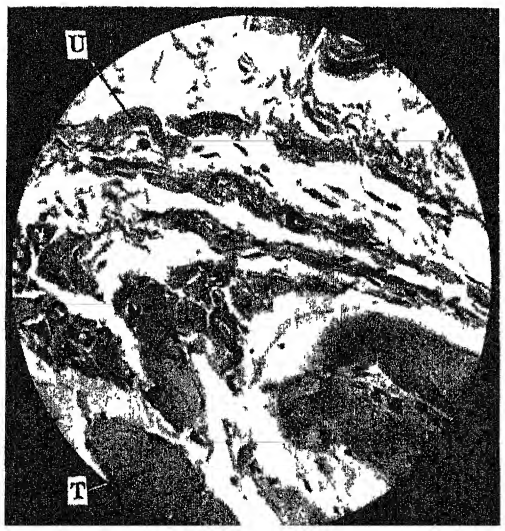
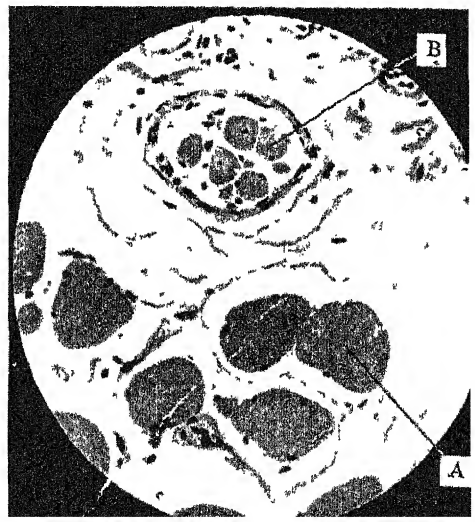


FIG. 7





[illegible]

CALCAREOUS DEGENERATION OF THE HEART AND OTHER ORGANS.

FIG. 1.

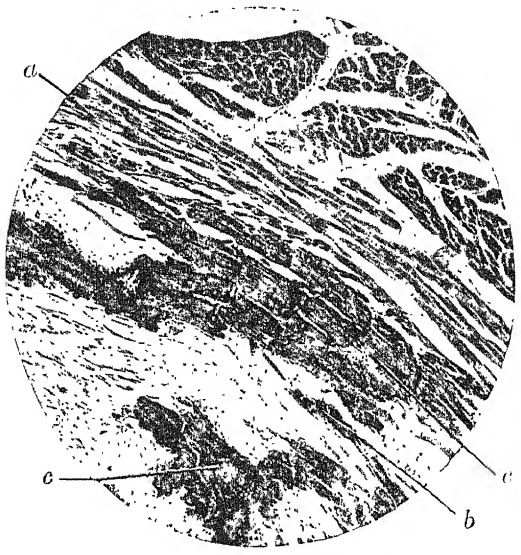


FIG. 2.

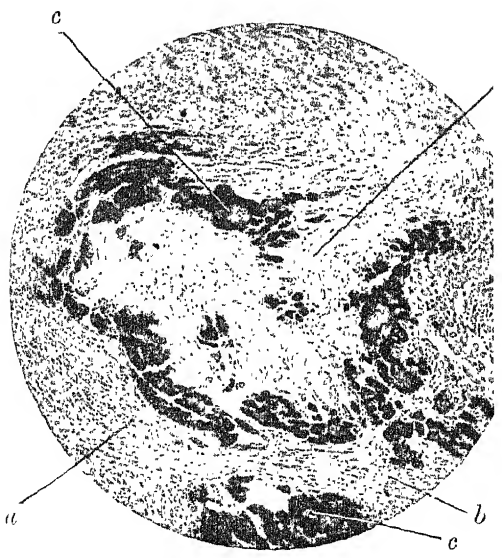


FIG. 3.

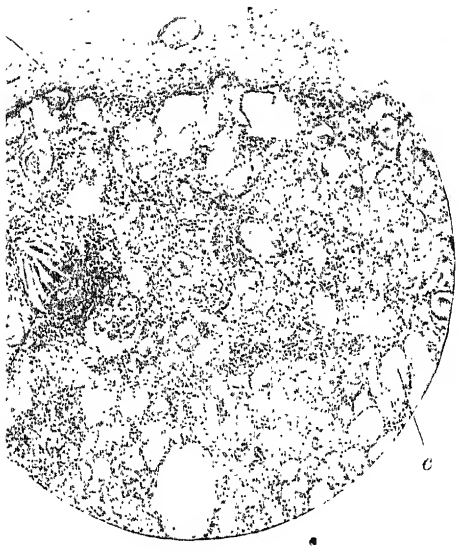


FIG. 4.

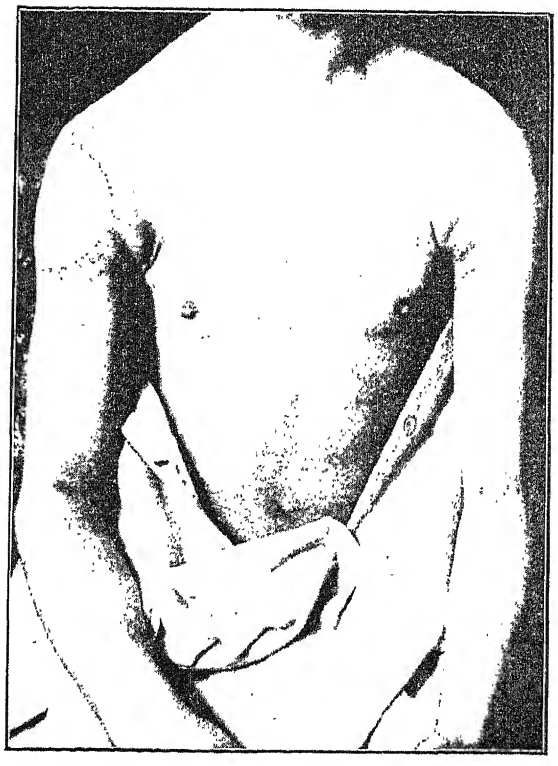


FIG. 9.

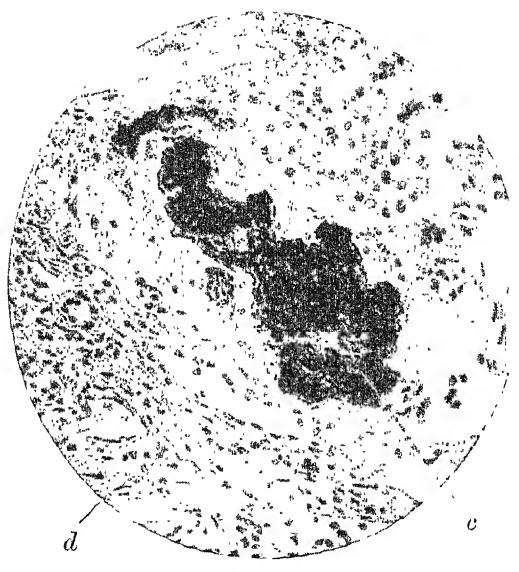


FIG. 5.

FIG. 7.

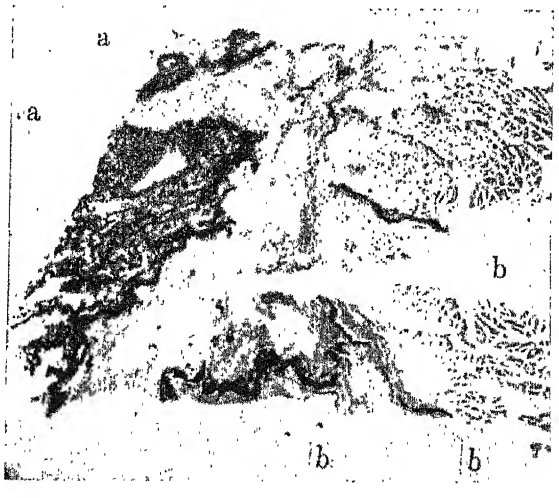
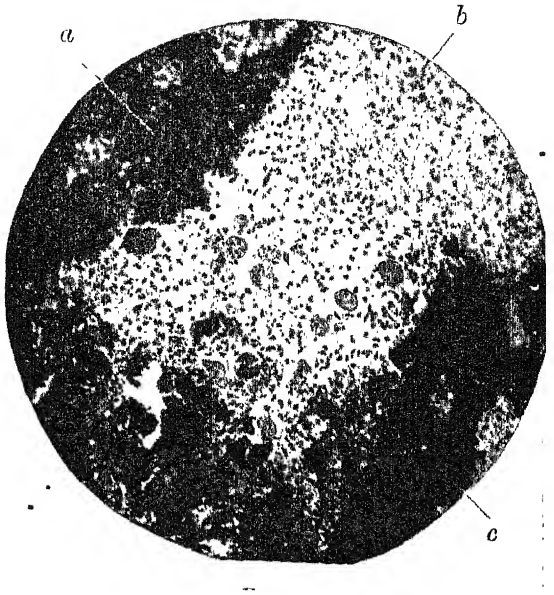


FIG. 6.



PERNICIOUS ANÆMIA.

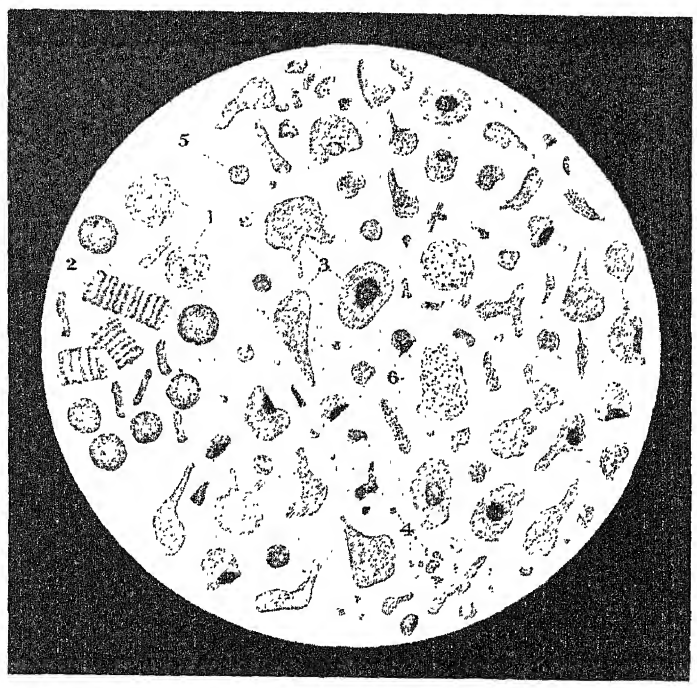


FIG. 1.

DIAGRAM OF THE BLOOD IN IDIOPATHIC OR PERNICIOUS ANÆMIA, VERY HIGHLY MAGNIFIED.

The red corpuscles are markedly altered in size and shape, and some of them appear to be nucleated.

The number 1 points to two normal white corpuscles; 2, to normal red blood corpuscles; these have been placed in the figure for the purpose of comparison. The number 3 points to large red corpuscles, two of which are markedly irregular in shape, and one of which appears to be nucleated. The nucleation in this and many of the other red corpuscles represented in the drawing is apparent only, and due to a condensation of the hæmoglobin in one part of the corpuscle.

The number 4 points to three very minute masses of protoplasm, which appear to be of the same composition as the red blood corpuscles, and which are perhaps very minute red blood corpuscles.

The number 5 points to a small deeply coloured red corpuscle. These are not always present in Idiopathic Anæmia, but when present are, I believe, of considerable diagnostic value.

The number 6 points to a large mass of granular material, evidently of the same composition as the white blood cells.

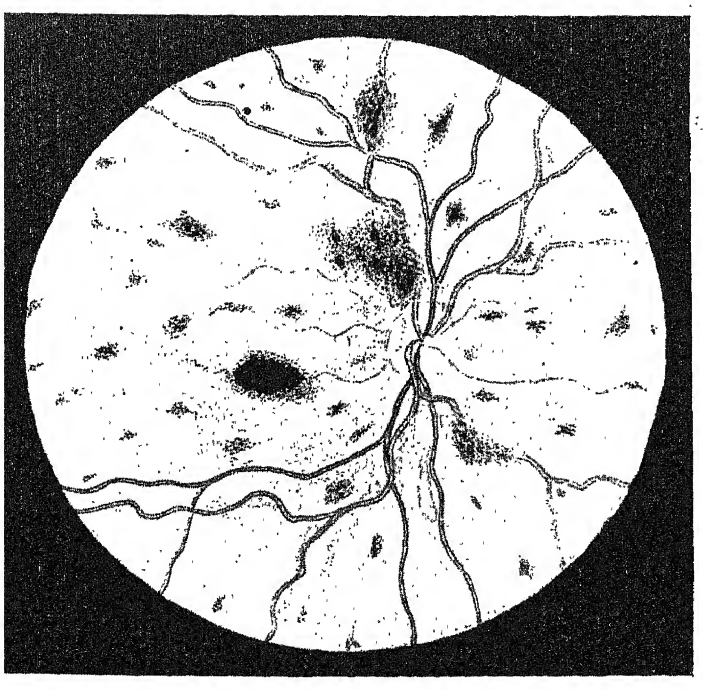


FIG. 2.—Fundus oculi in a case of pernicious anæmia showing numerous retinal hæmorrhages. The optic disc is very pale, but otherwise normal. Some of the hæmorrhages are of considerable size. Some of the larger vessels are surrounded by hæmorrhages.

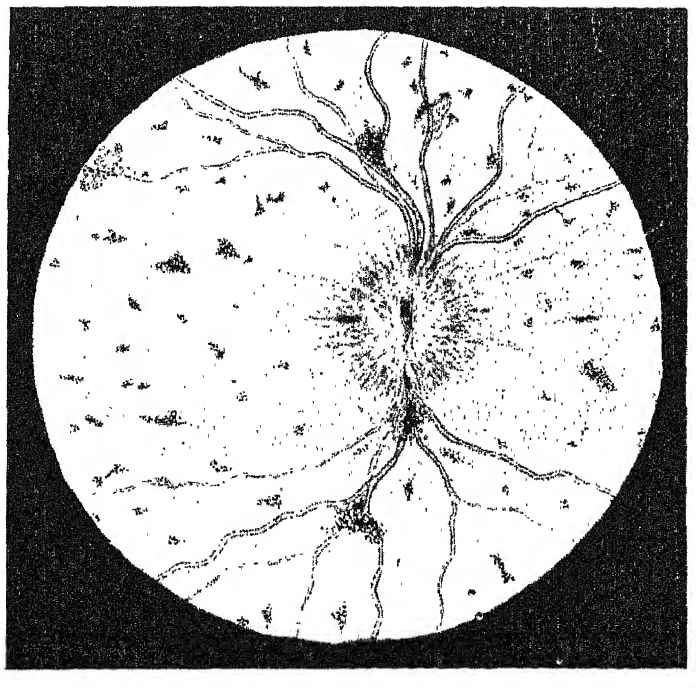


FIG. 3.—Fundus oculi in a case of pernicious anæmia showing papillitis with small flame-like hæmorrhages in the margins of the optic disc, and numerous small hæmorrhages in the retina. Some of the larger vessels are surrounded by hæmorrhages.

ALOPECIA AREATA.

FIG. 1.

FIG. 2.

FIG. 3.

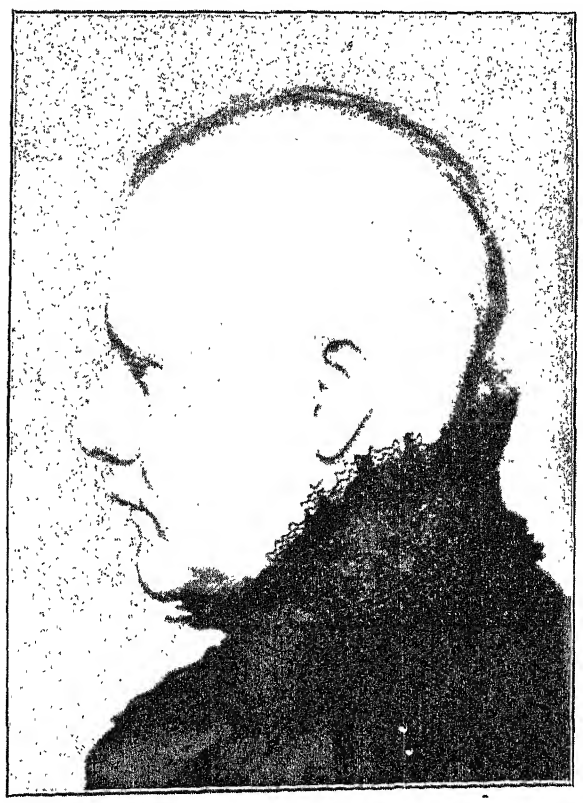
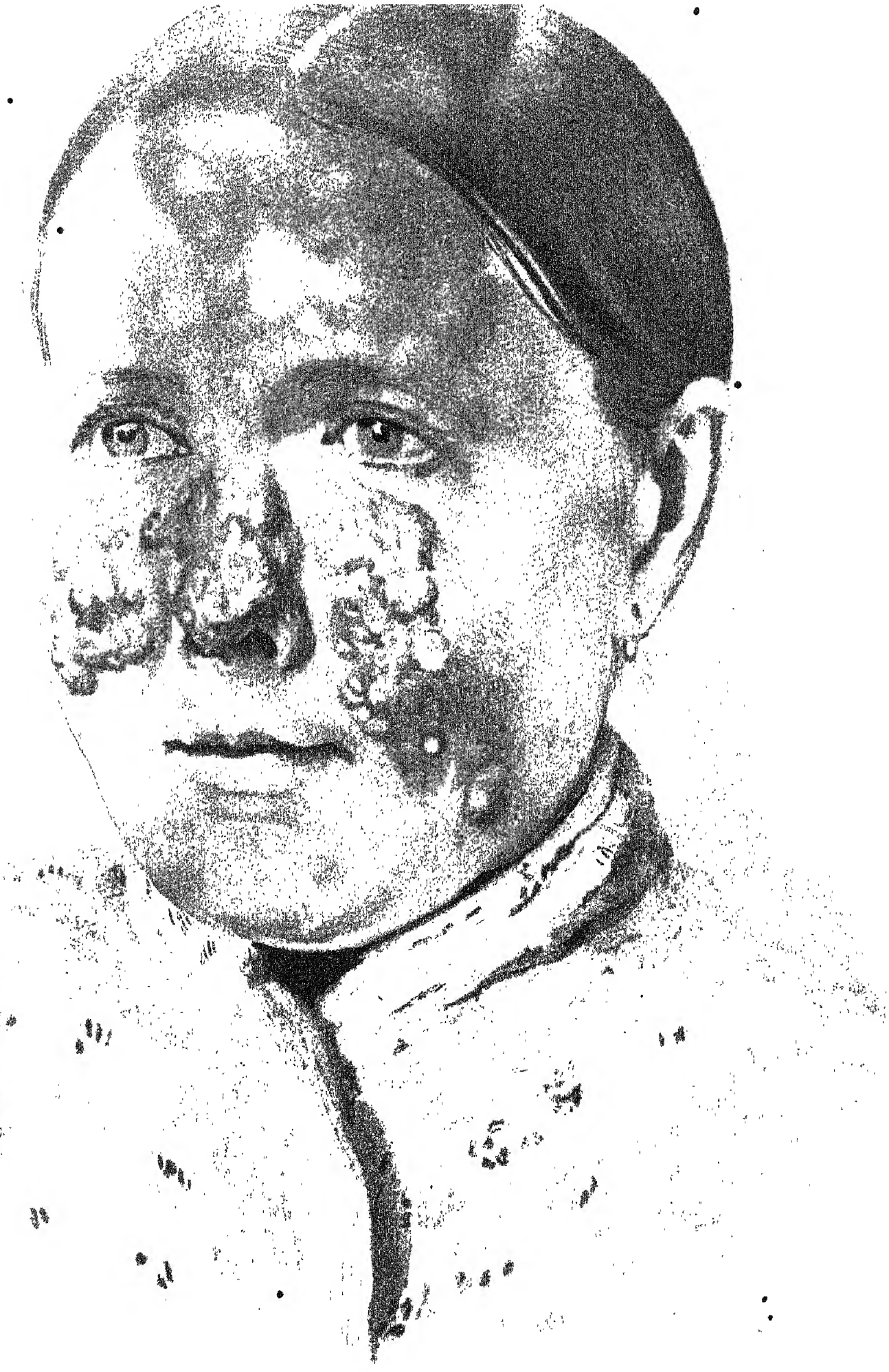


FIG. 4.



LUPUS VULGARIS